

FIGURE 1A

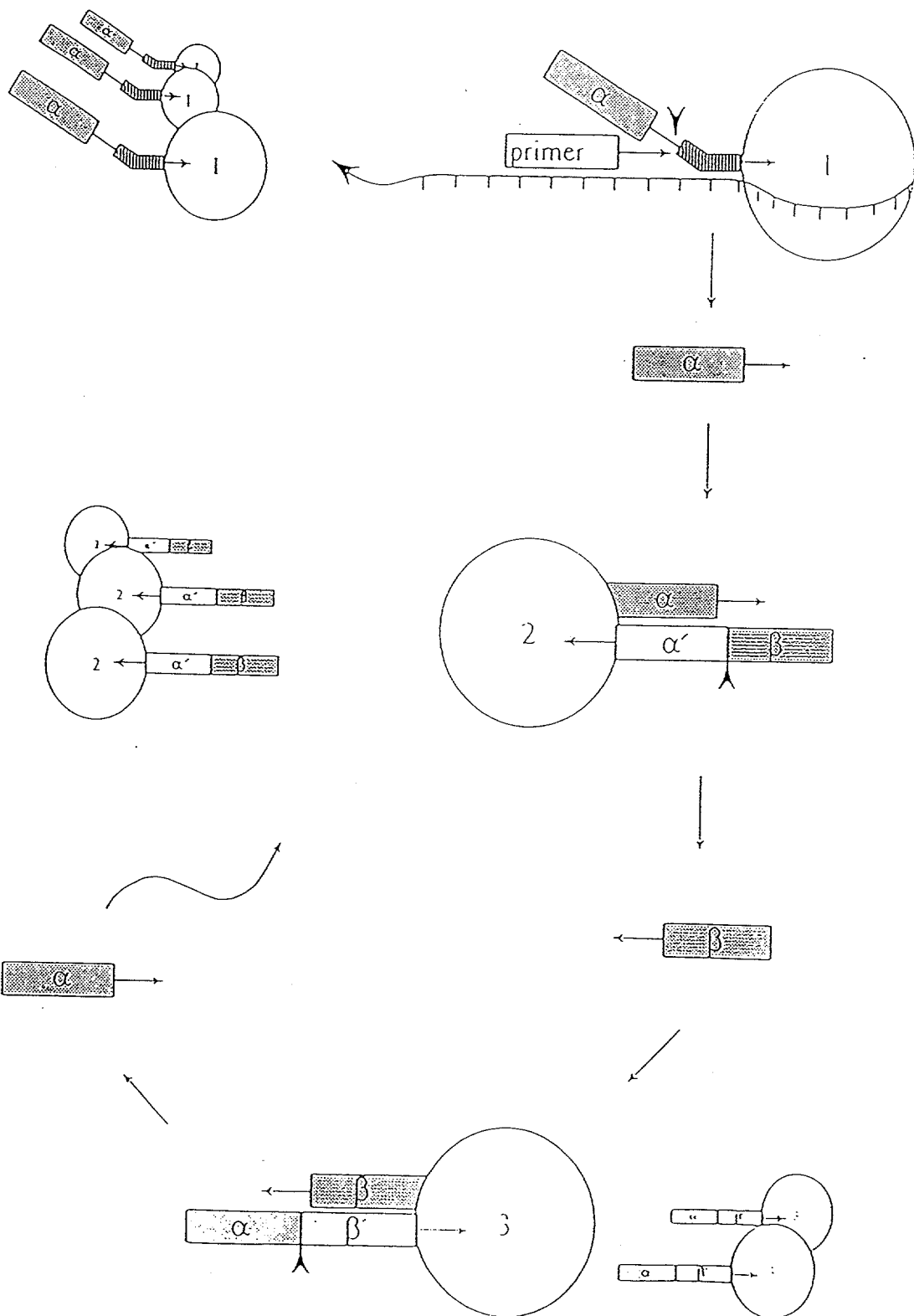
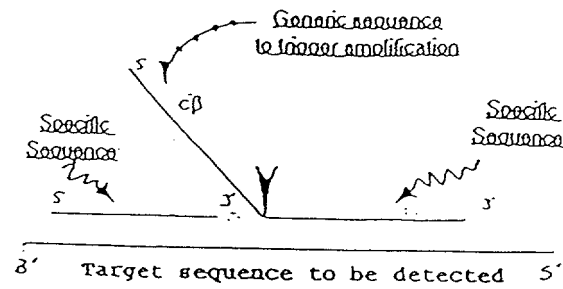


FIGURE 1B

PART ONE: TRIGGER REACTION



PART TWO: DETECTION REACTION

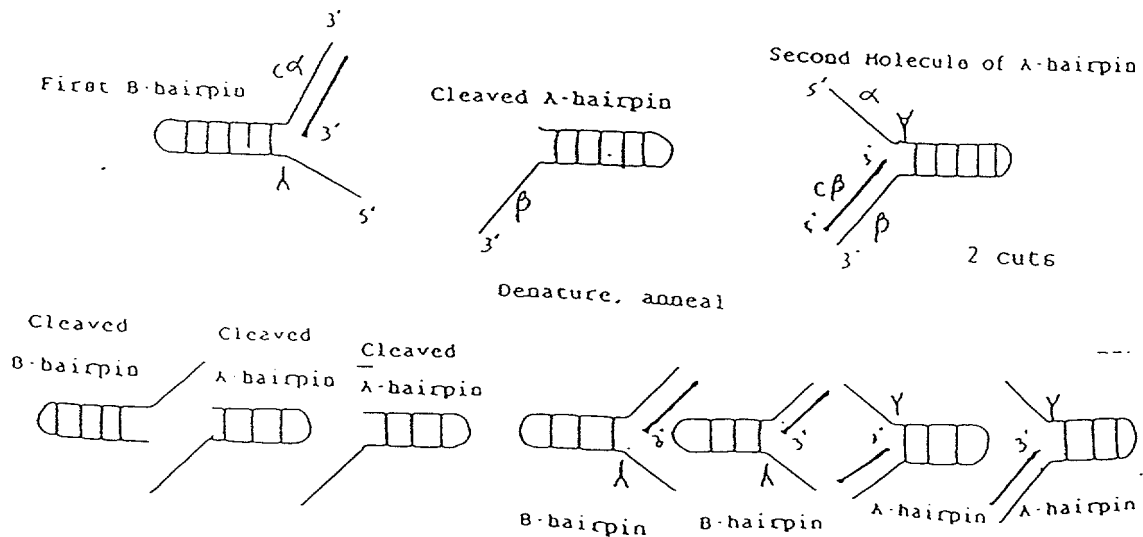
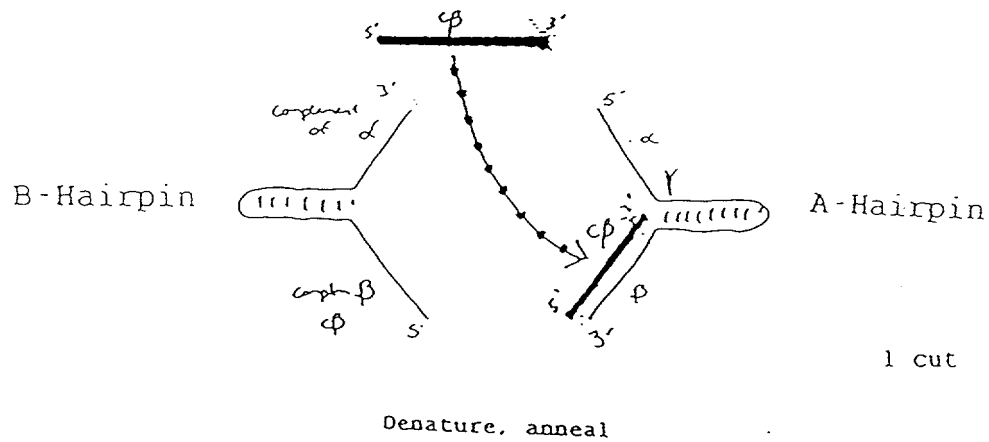


FIGURE 2 (cont'd)

MAJORITY (SEQ ID NO:7)	ICCAGCCCCACAI	CCAXCACCIC	AXGCCIC	ICCTGGAGC	IXICCCAGC	ICCCGAC	CCGAC	CCCGCC	CCGCA	764
ORAPTAO (SEQ ID NO:1)	I									
CHAPTR (SEQ ID NO:2)	GGG									761
CHAPTH (SEQ ID NO:3)	A									770
MAJORITY	GGTGGAC	TCGGCCAA	CGCCGCGA	CCCGGAC	CGCGCC	CTTACGGCC	CTTCTCGG	ACAGCC	CTCGCAC	
ORAPTAO										834
CHAPTR										831
CHAPTH										840
MAJORITY	GGCAGCC	CTCCAGC	AGTCCG	CCCTCC	CTCCAGC	CGCCCA	AGCCG	CCCTCCG	CCGCCCC	
ORAPTAO										904
CHAPTR										901
CHAPTH										910
MAJORITY	CCGAA	CGCCGCT	TCGTCC	CTTCCG	CTTCCG	CGCCGAC	CGCCCA	TCGTCCG	CGCCGCT	
ORAPTAO										974
CHAPTR										971
CHAPTH										980
MAJORITY	CCCCG	CCAGC	CGCCGCT	CCAC	CGCCG	CCAGC	ACCCCT	TTXCGG	CCCTXAGC	
ORAPTAO										1044
CHAPTR										1041
CHAPTH										1050

FIGURE 2 (cont'd)

MAJORITY	(SEQ ID NO:7)	CCCCGXCTCCCTCCCCAAGCACCCTGCCCGCTTTCGCCCTCAGCGACGCCCTXCACCCTCXTCGCCCGCCACCG
OKAPTAO	(SEQ ID NO:1)C..T.....A.....AG.....C.....A.....T..G.....CC.....C.....
OKAPTR	(SEQ ID NO:2)AA.....G.....G.....C.....C.....T..C.....A..A.....
OKAPTH	(SEQ ID NO:3)C.....C.....C.....C.....TC.....G..A.....G.....
MAJORITY		ACCCCACTCCCTCCCTACCTCCCTCCGACCCCTCCACACACCCCGCCGCTGCCCGCCCGCTACCG
OKAPTAO	G.....T.....T.....
OKAPTR	G.....T.....T.....
OKAPTH	G.....T.....G.....
MAJORITY		CCCCGACTCCGACCGCAGCAXCCCGCGCGAGCGCGCGCTCCCTXTCGACAGCGCTCTCCXGACCTXXXCAG
OKAPTAO		C.....G.....G.....CC.....T.....GCC.....GCC.....CTG..G..125
OKAPTR	T.....A.....CC.....G..C.....A..C.....AA..125
OKAPTH	C..C..CCC..C.....C..G.....CAT..G.....CCCTA..128
MAJORITY		CCCCCTCAGCGCGCAGCAGCAGCTCCCTTCGCTTACCACGAGCTCCACAGCCCTTCCCGCTCCCT
OKAPTAO		A..C.....A.....A.....A.....G.....G.....CCCT.....132
OKAPTR	A.....A.....AC..C..G.....G.....G.....CT.....132
OKAPTH	C.....A.....A.....C.....C.....A.....G.....133
MAJORITY		CCACACTCCAGCCCGCCCGCTXCCGCTCCGACCTGCCCTACCTCCAGCGCCCTXTCCTCCAGCTCCCGCA
OKAPTAO	G..C.....G..C.....T.....AG.....T..G.....C.....139
OKAPTR	CC.....C.....C.....C.....C.....A..C..139
OKAPTH	C.....A.....A.....T.....T.....C..T.....140

Table 1. Demographic characteristics of the study population	
Age (years)	Mean (SD)
Male	55.2 (10.5)
Female	56.8 (11.2)
Marital status	
Married	78.5%
Single	21.5%
Education level	
High school or above	65.2%
Below high school	34.8%
Occupation	
White collar	45.1%
Blue collar	54.9%
Income (USD/month)	
< 1000	12.3%
1000-2000	35.7%
> 2000	52.0%
Health insurance	
Yes	89.1%
No	10.9%
Comorbidities	
Hypertension	32.1%
Diabetes	18.5%
Cholesterol	25.3%
Smoking status	
Current smoker	15.2%
Former smoker	28.7%
Non-smoker	56.1%
Alcohol consumption	
Regular	8.9%
Occasional	22.4%
None	68.7%

FIGURE 2 (cont'd)

[illegible]

FIGURE 2 (cont'd)

MAJORITY	(SEQ ID NO:7)	ACAAACAICCCCGTCCGCCACCCXCTGCCCCACAGCAATCCGCCCGGCCCTCCGTCGCCCCACGACGCCXTC	1814
ORAPTAO	(SEQ ID NO:1)G..I..G.....A..C.....C.....	1814
ORAPTR	(SEQ ID NO:2)G.....I.....C..C.....A.....C.....	1811
ORAPTH	(SEQ ID NO:3)CI.....C.....C.....C.....I.....C.....	1812
MAJORITY		CTTGGTGGCCCTGGACTATAGCCAGATAGAGCTCGGGCTCGTCCGCCACCTCTCCGGGGCAGCAGACCTC	
ORAPTAO		A.....I.....I.....C.....A.....G.....C.....	1884
ORAPTR	I.....I.....C.....I.....I.....C.....	1881
ORAPTH	C.....C.....C.....C.....C.....A.....	1890
MAJORITY		ATCCGGCTCTTCCAGCAGCGGAGCGGACATCCACAGCCAGACCCGCCAGCTGGATCTTCCGGCTCCCGCCCG	
ORAPTAO	I.....I.....C.....G.....G.....G.....	1954
ORAPTR	A.....I.....A.....A.....I.....C.....	1951
ORAPTH	A.....A.....A.....A.....A.....C.....	1960
MAJORITY		ACGCCCTGCACCCCTGATGCCCGCGCGCGCGCGCGCAACATCAACCTCCCTCTACCGGCACTCTCCCG	
ORAPTAO	A.....A.....I.....G.....G.....G.....	2020
ORAPTR	A.....A.....I.....G.....G.....G.....	2021
ORAPTH	A.....A.....I.....G.....G.....G.....	2030
MAJORITY		CCACCGCCCTCTCCAGGAGCTTCCCATCCCGCTACGAGGAGCGCGCTTCCCGCTTCACTCAGCGGCTACCTCCAG	
ORAPTAO	A.....A.....I.....I.....I.....CCA.....I.....	209
ORAPTR	A.....A.....I.....I.....I.....CCA.....I.....	209
ORAPTH	A.....A.....I.....I.....I.....CCA.....I.....	2100

[illegible]

FIGURE 2 (cont'd)

[illegible]

9/127

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2423	2424	2425	2426	2427	2428	2429	2430	2431	2432	2433	2434	2435	2436	2437	2438	2439	2440	2441	2442	2
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FIGURE 2 (cont'd)

MAJORITY	(SEQ ID NO:7)	CCCCCTGGAGCTCGACCTGGCGCATGGCGGAGGCACTGGCTCTCCGCCAACGACTAG
ONAPTAO	(SEQ ID NO:1)A.....CA
ONAPTR	(SEQ ID NO:2)CC.....
ONAPTH	(SEQ ID NO:3)T.....CT

2498 2498 2505

FIGURE 3

MAJORITY (SEQ ID NO:8)	HXAMHPLFEPKCAVLLVDOCHLAYRTFFALKOLTTSRCEPVDAVYGFAKSLIKALKKEOC OAVXVVFQAK	
1A0 PRO (SEQ ID NO:4)	RC	H
TR PRO (SEQ ID NO:5)		I
TTX PRO (SEQ ID NO:6)	E	V V
		YK F
		7L
MAJORITY	APSFRAHEAYEAYKACRAPTPEDFPROLALIKELVOLLCLXRLEVPCEADDOVLATLAKKAEKECEYEVRII	
1A0 PRO	CG	A
TR PRO		S
TTX PRO		R
		13
		13
		14
MAJORITY	TADROLYOLLSDRIAVLHPEGYLITPAWLWEKYGLRPEOWVOYRALXGOPSONLPCVKCICEKIXKLIX	
1A0 PRO	K	T
TR PRO		R
TTX PRO		OR IR
		L K
		2
MAJORITY	EWGSLHLLKHLORVKP XXREKIXAHMEDLXLSXXLSXVATOLPLEVOFAXAREPOREGLRAFLE	
1A0 PRO	A	K
TR PRO	FOH O	GR T HL
TTX PRO		L OG
		2
		2
		2
MAJORITY	CSLLHEFOLLXPKALEEAPWPPPECAFVCFVLSRPEPMHAEILLALAPARXCRVHRAAXOPLXCLROLKEV	
1A0 PRO	S	PE YKA
TR PRO	C A	C WE L O R
TTX PRO	A AP	K C D A A K
		3
		3
		3

[illegible]

FIGURE 3 (cont'd)

MAJORITY (SEQ ID NO:8)

100880 (SEQ ID NO:4)

R000 (SEQ ID NO:5)

000000 (SEQ ID NO:6)

RGCLAKOLAVLALAEGLDLXPGDDPHLLAYLLOPSHTTPEGVAARYGCEWTEOACERALLSERLFXH
S. C. P. E. A. A. WC
I. F. E. A. OI. XE
S. V. AH. HR. LX 420

ՀԱՅՈՑՈՒՄ

0880

11

82

[illegible]

ՀԱՅՈՐՄԻ

150 880

১৯৯৫

22

0LERVLFOELGLPAICXTEKTKRSTSAAVLEALREAHPIVEKILQYRELTKLKNTYIDPLPXLVHPRIG
SS8
SS7
S6C

MAJORITY

089 061

ମା

മുഖ്യ

RLHT8FNOTATATCRLSSSDPHLOHI PVRTPLCGRIRRAFAVEECWXLVALDYSOI ELAVLAHL SGO

621
62.
62
63

152087

12080

12

88

1	RVFOEGROI	HTOTASWMF	CVPPEAVOPL	MARRAAKTI	HFGLVYCHSAHLSOELAI	PYEAAVAFI	ERYFO
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82							

FIGURE 4

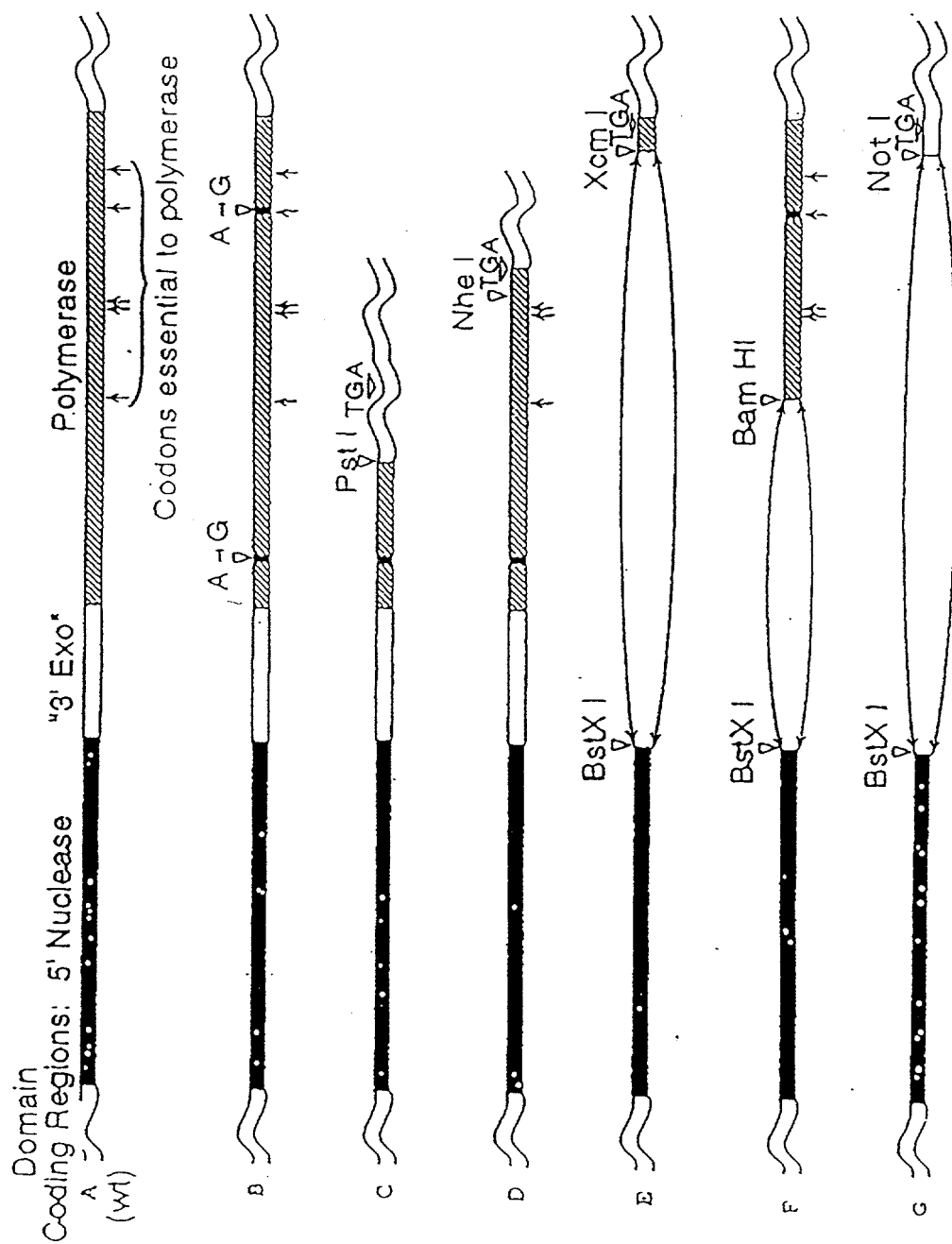
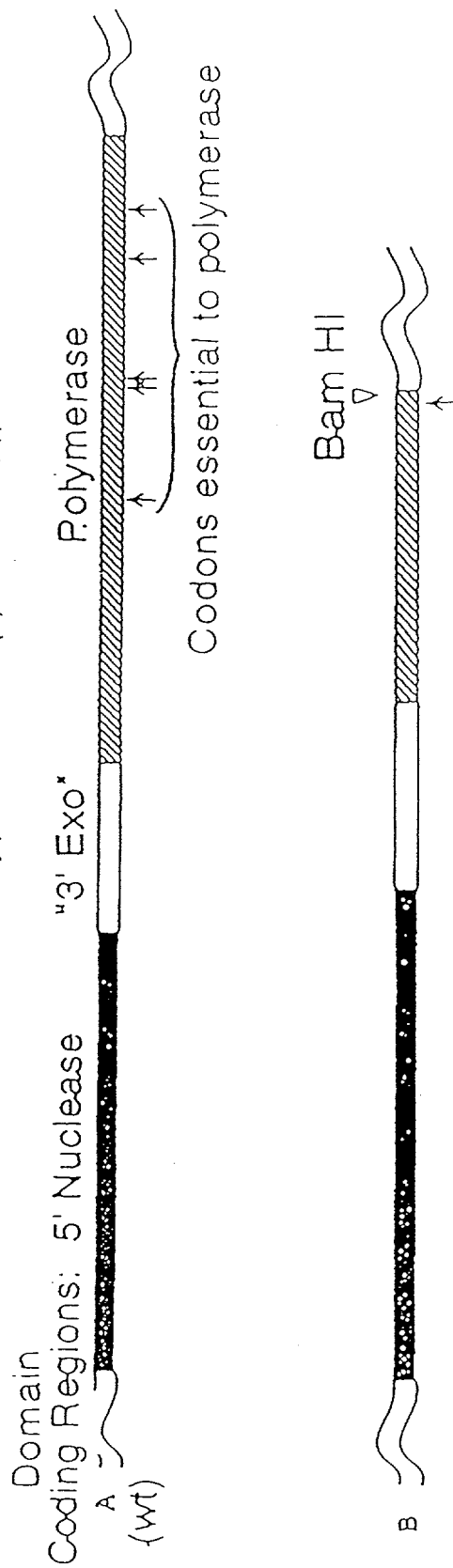


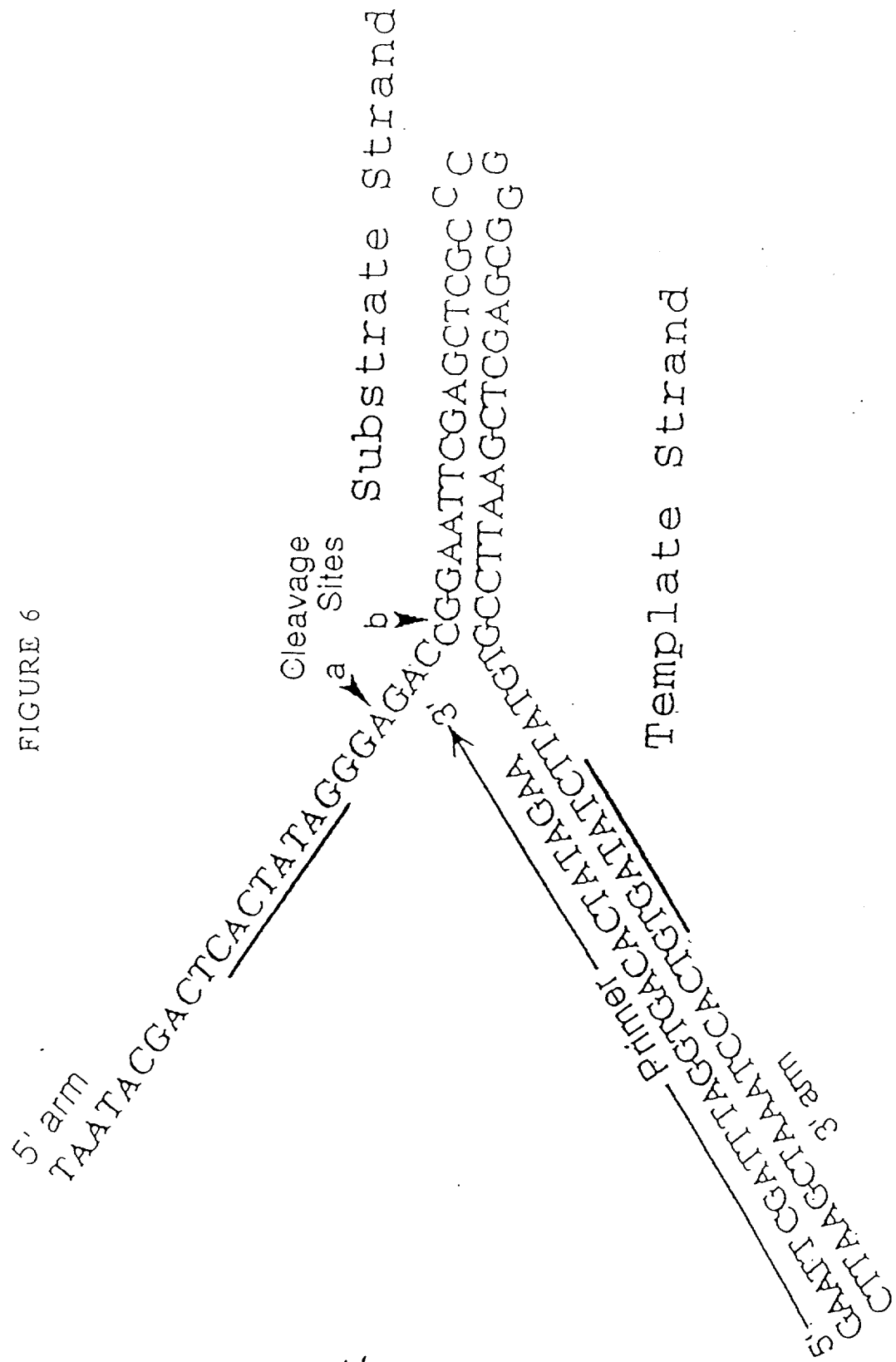
FIGURE 5

Genes for Wild-Type and Pol(-) DNAPT^H



009007 50E48960

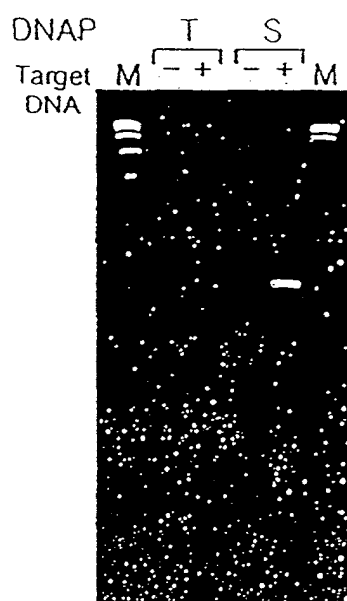
FIGURE 6



16/127

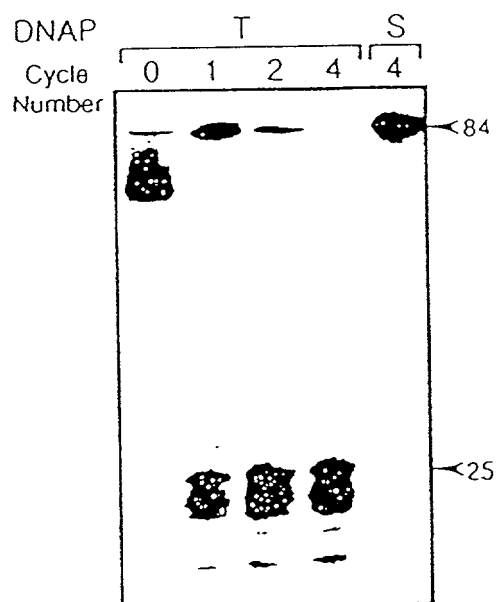
09684305.100600

FIGURE 7



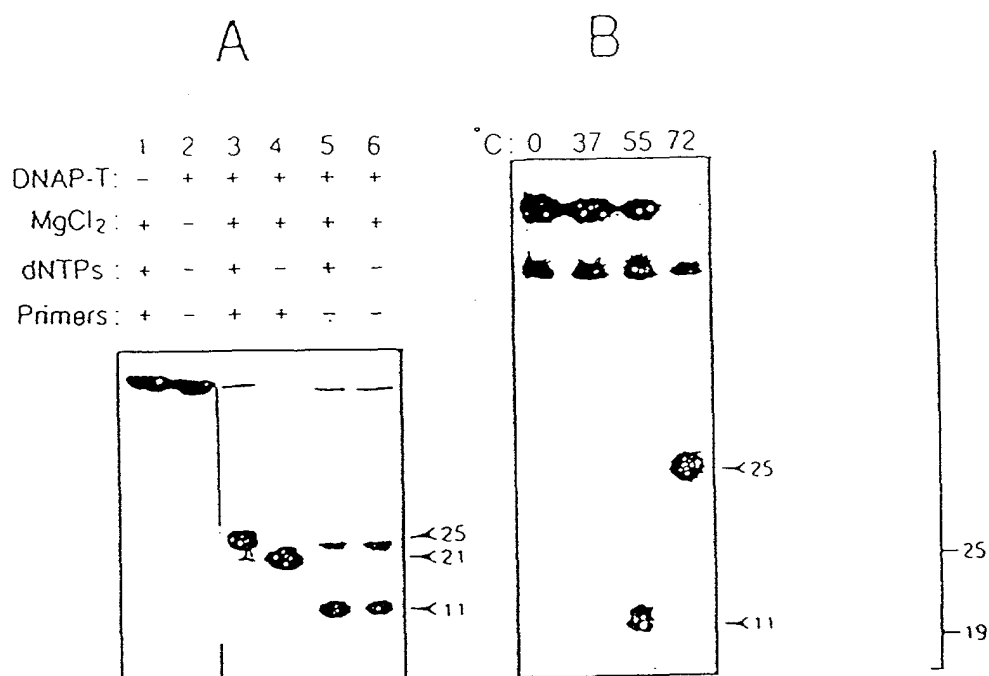
00604905-100600

FIGURE 8



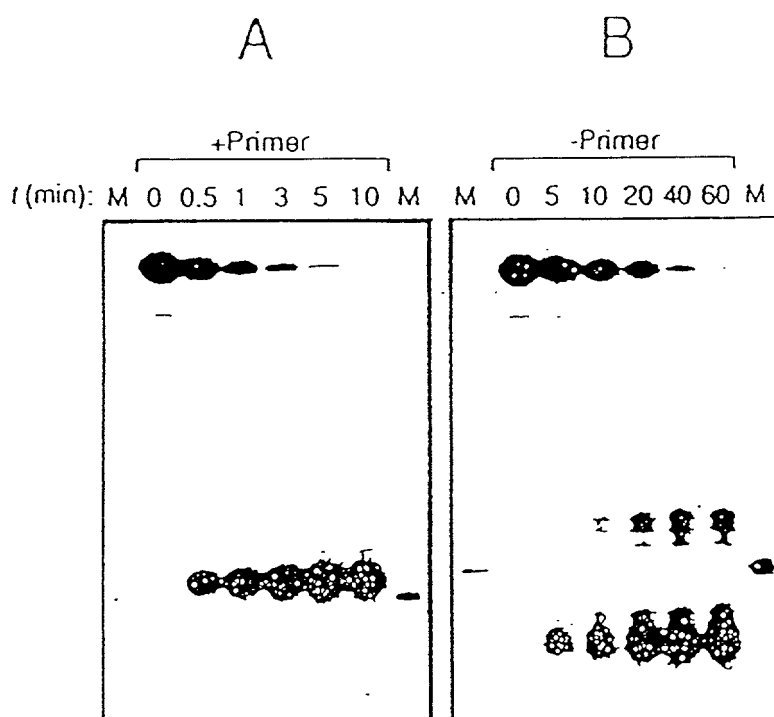
09684305-100600

FIGURE 9



006498-10600

FIGURE 10



000007" 50E+12560

FIGURE 11

A B



21/127

1. The first step is to identify the problem. This involves understanding the situation, gathering information, and defining the problem clearly.

22/127

A

Substrate DNA (206 nt)

5' ACCGAAACACACCAATACCAATCAATACGCCAAGCT →

3' CCGATCGCTTACCTAATGCT

19.12

B

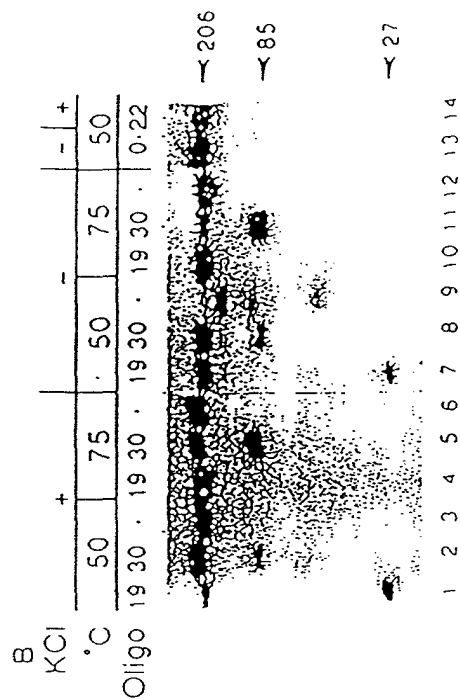
Substrate DNA (206 nt)

5' AACCTCCCAATCCCTCCAGGTCACATCTACAGGATCCC →

3' CCGTACCGGAGCTCCAGGTCGAGATCTCCTAGGCT

30.12

FIGURE 12



009007" 50E49360

FIGURE 13

23/127

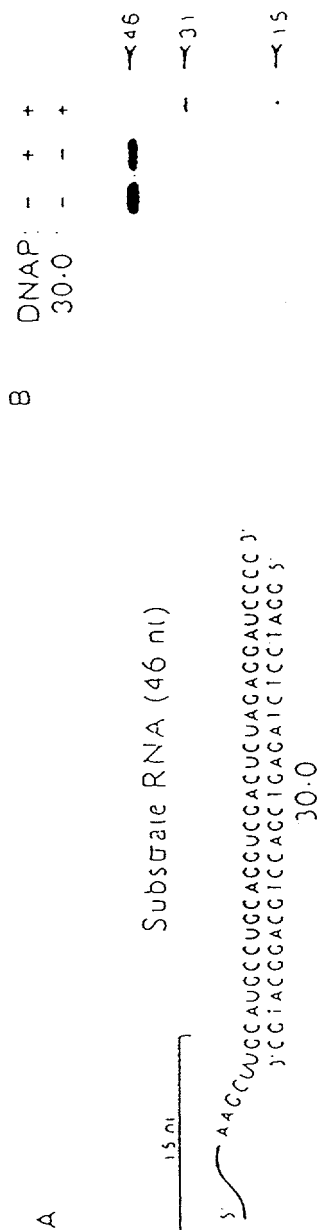
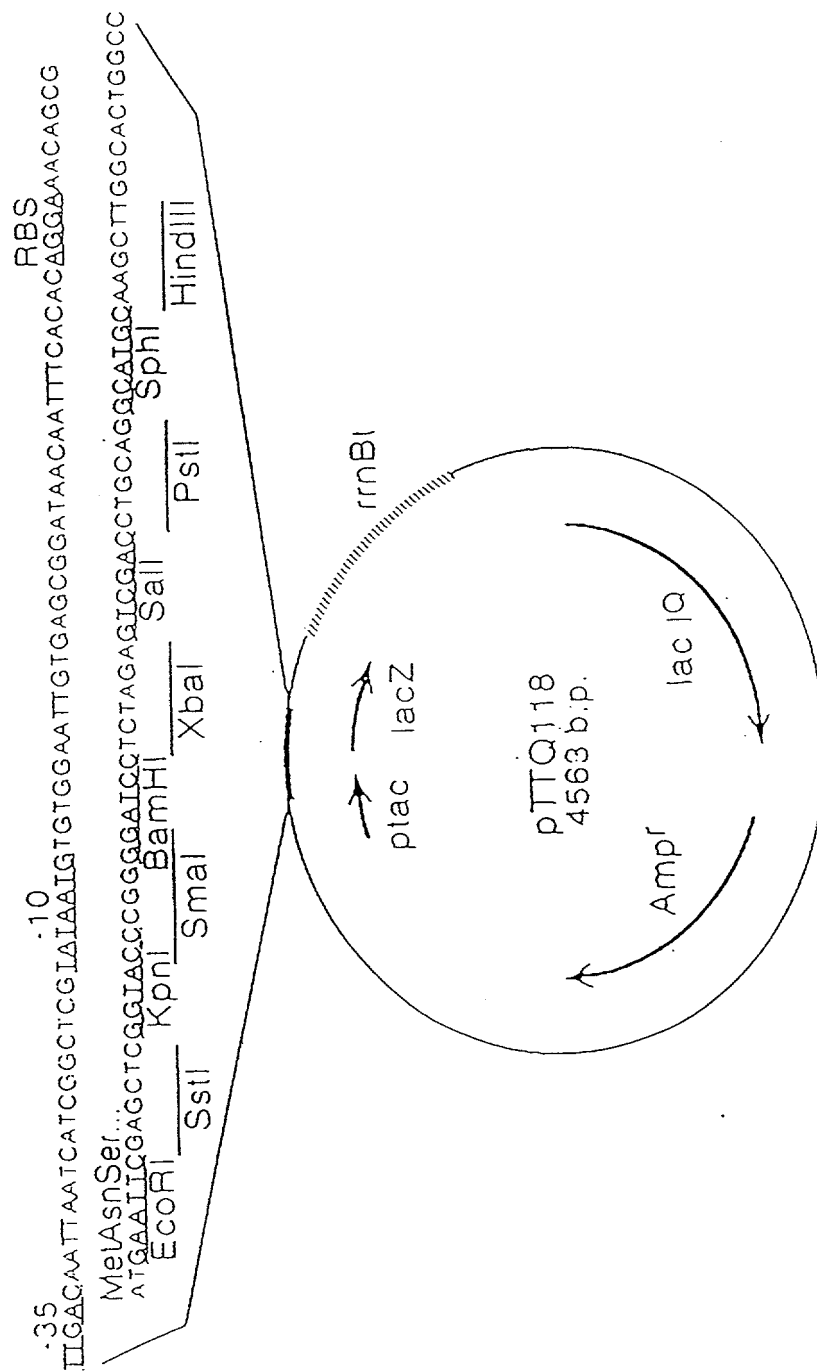
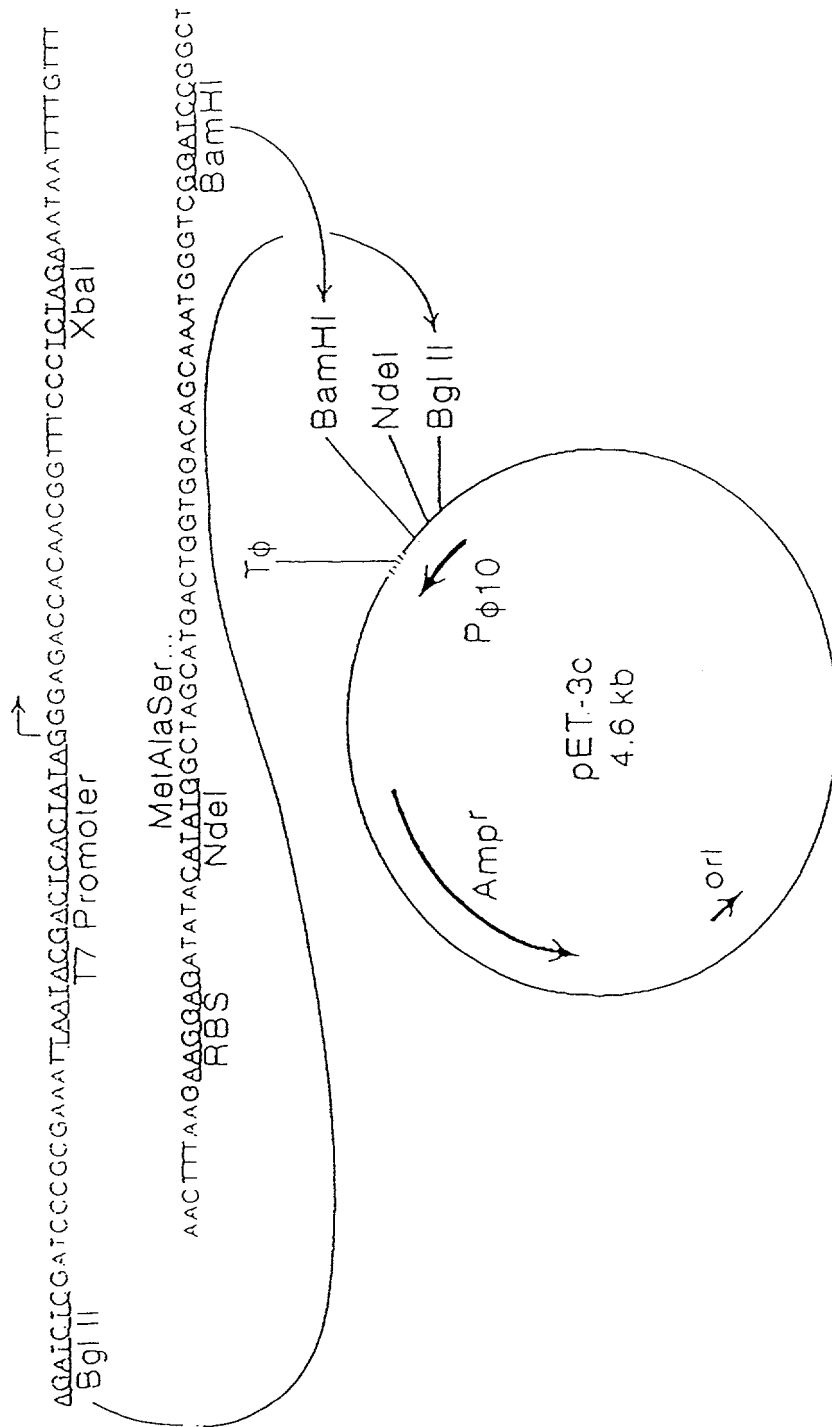


FIGURE 14



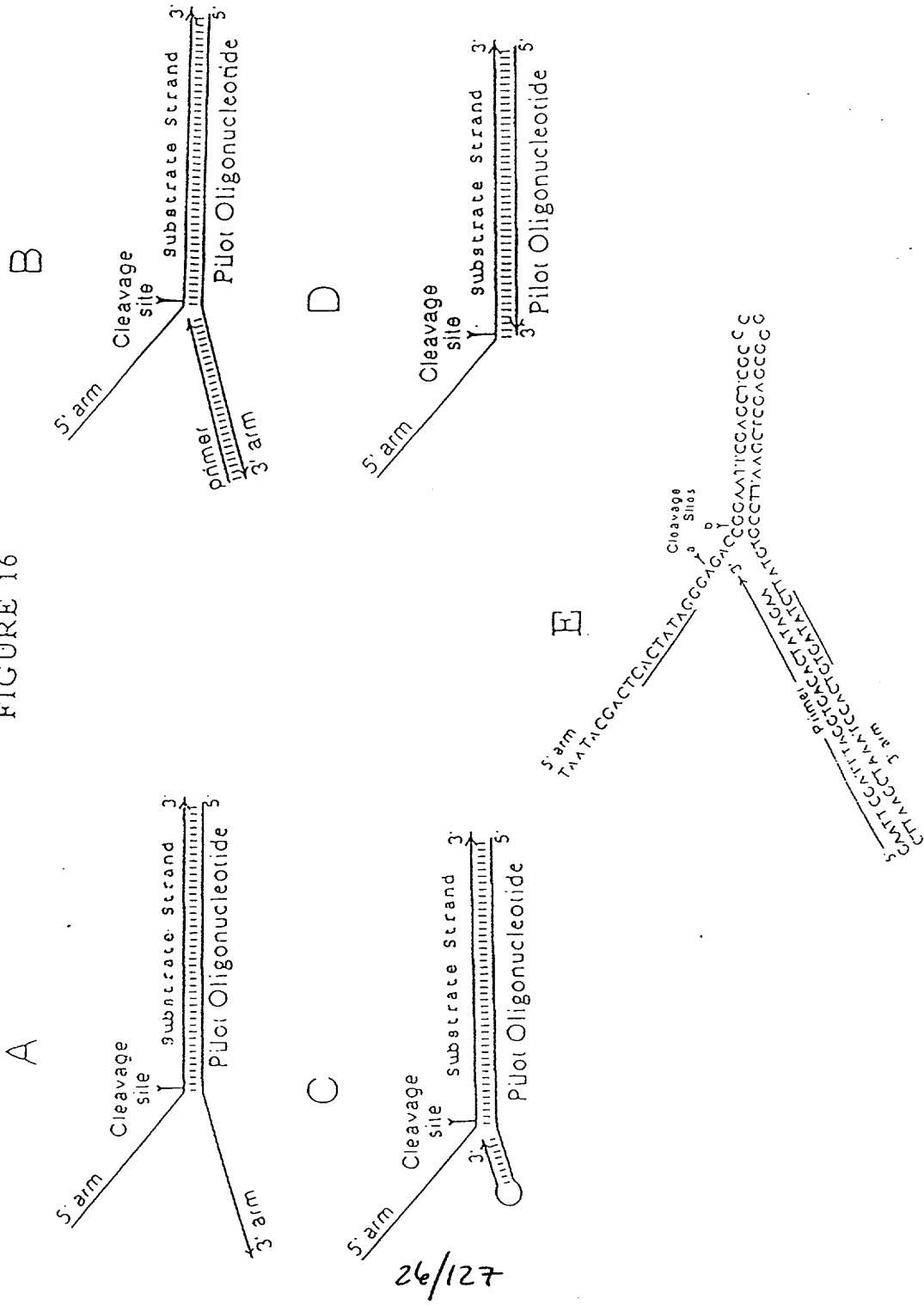
RBS: Ribosome binding site
 plac: Synthetic lac promoter
 lacIQ: Lac repressor gene
 lacZ: Beta-galactosidase alpha fragment
 rrnBI: E. coli rrnB transcription terminator

FIGURE 15



P_{φ10}: Bacteriophage T7 $\phi 10$ promoter
 T ϕ : T7 ϕ Terminator
 RBS: Ribosome binding site


FIGURE 16




000001 5054950

FIGURE 17

1 2 3 4 5 6 7

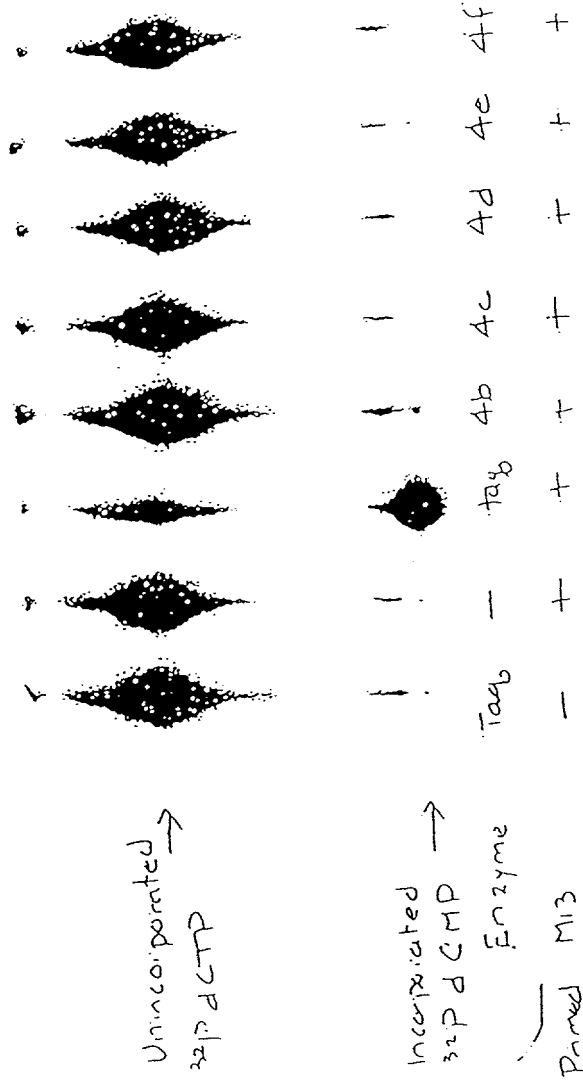
] Uncleaved substrate

 Cleaved substrate

-	-	-	+	-	-	+	dNTPs
-	-	+	+	-	-	+	Primer
Reg	4e			5b			Enzyme

009001" 50E+09960

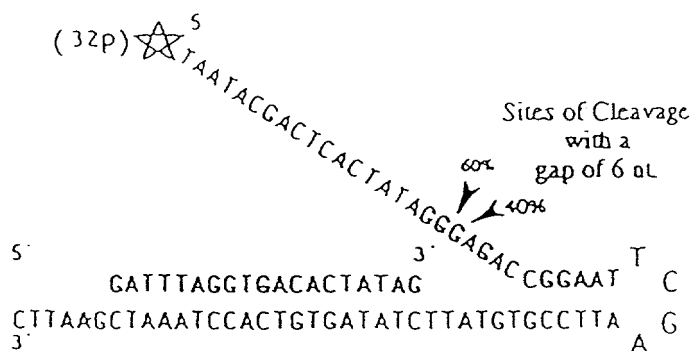
FIGURE 18



09684305-100600

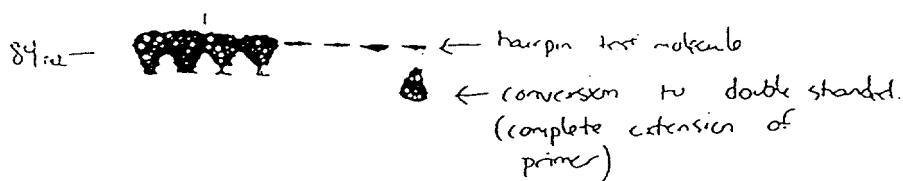
FIGURE 19

A

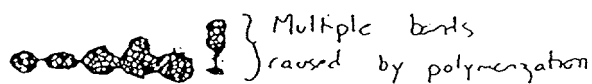


B

		"4d"		"4b"			
		No (2 pr. mutation)		Unmodified			
		Pr. activity		small activity		DNM Tag	
1	2	3	4	5	6	7	8
		C		T		T	
		+		-		+	
						MTP	



desired product
21 nt

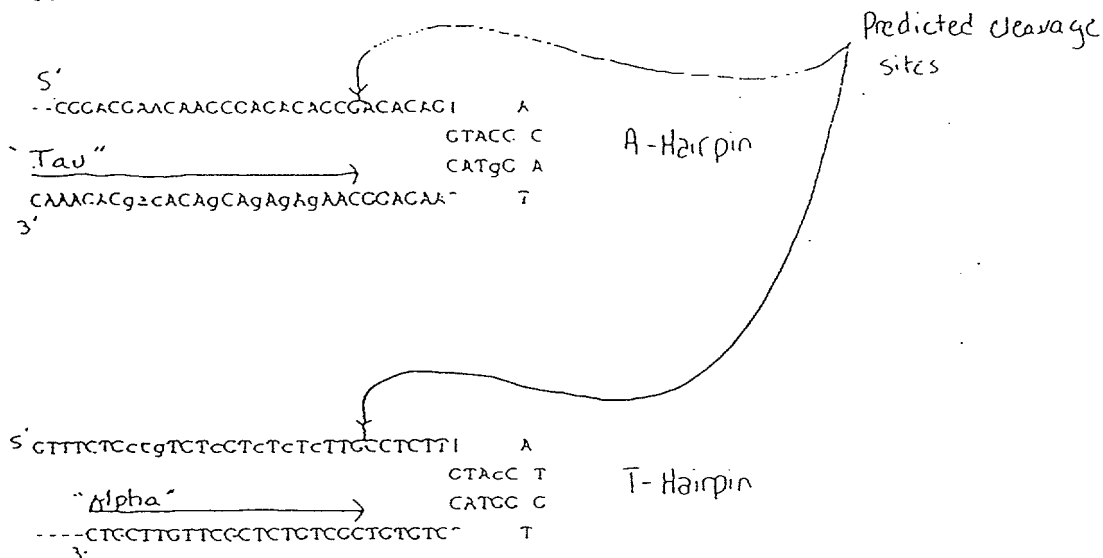


↑ some aberrant cleavage with "4b" because of residual polymerase activity

29/127

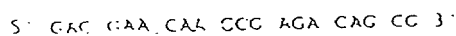
FIGURE 20

A

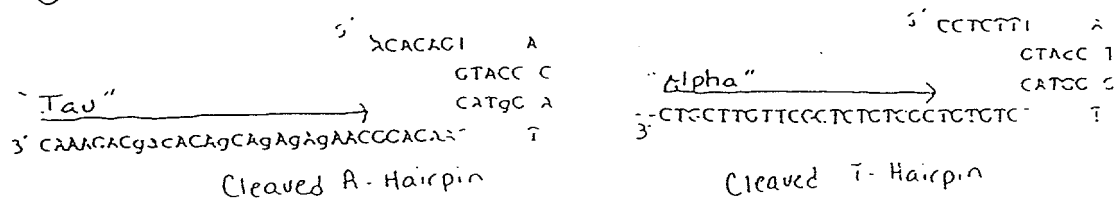


B

Sequence of alpha primer:



C



D

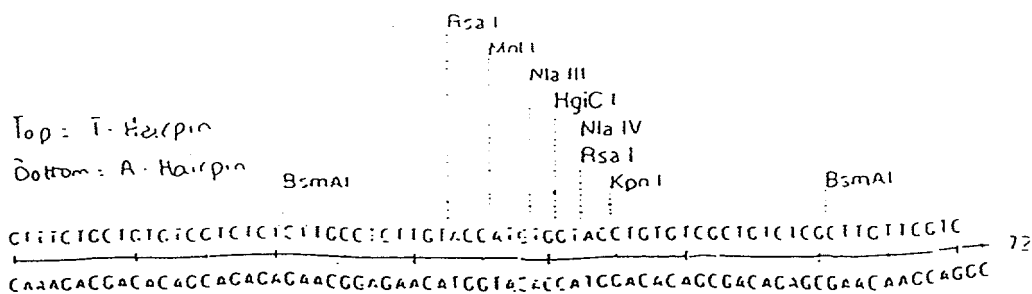
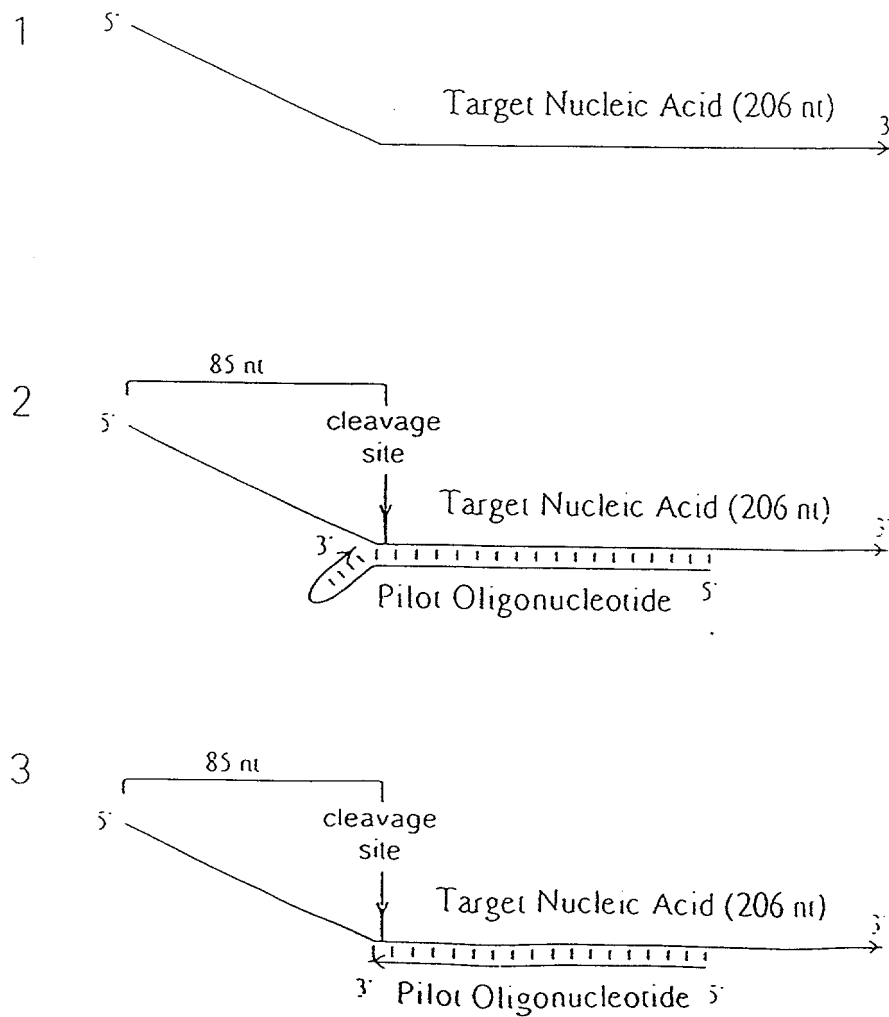


FIGURE 22A



009007" 50E43960

FIGURE 22B

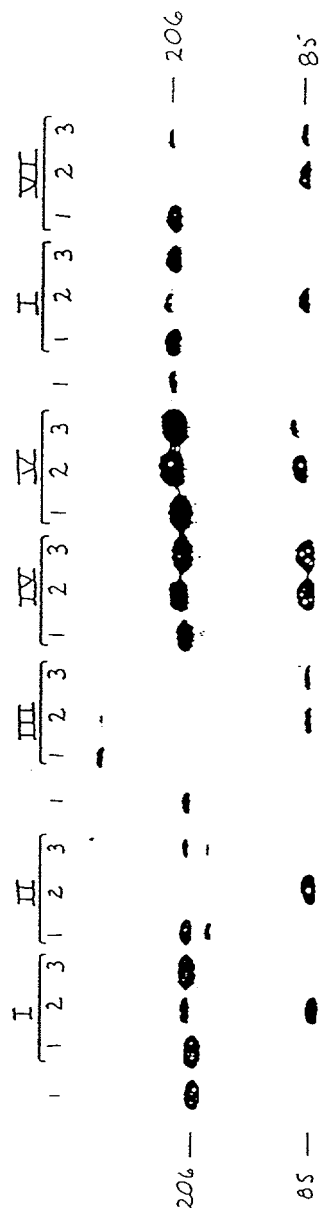
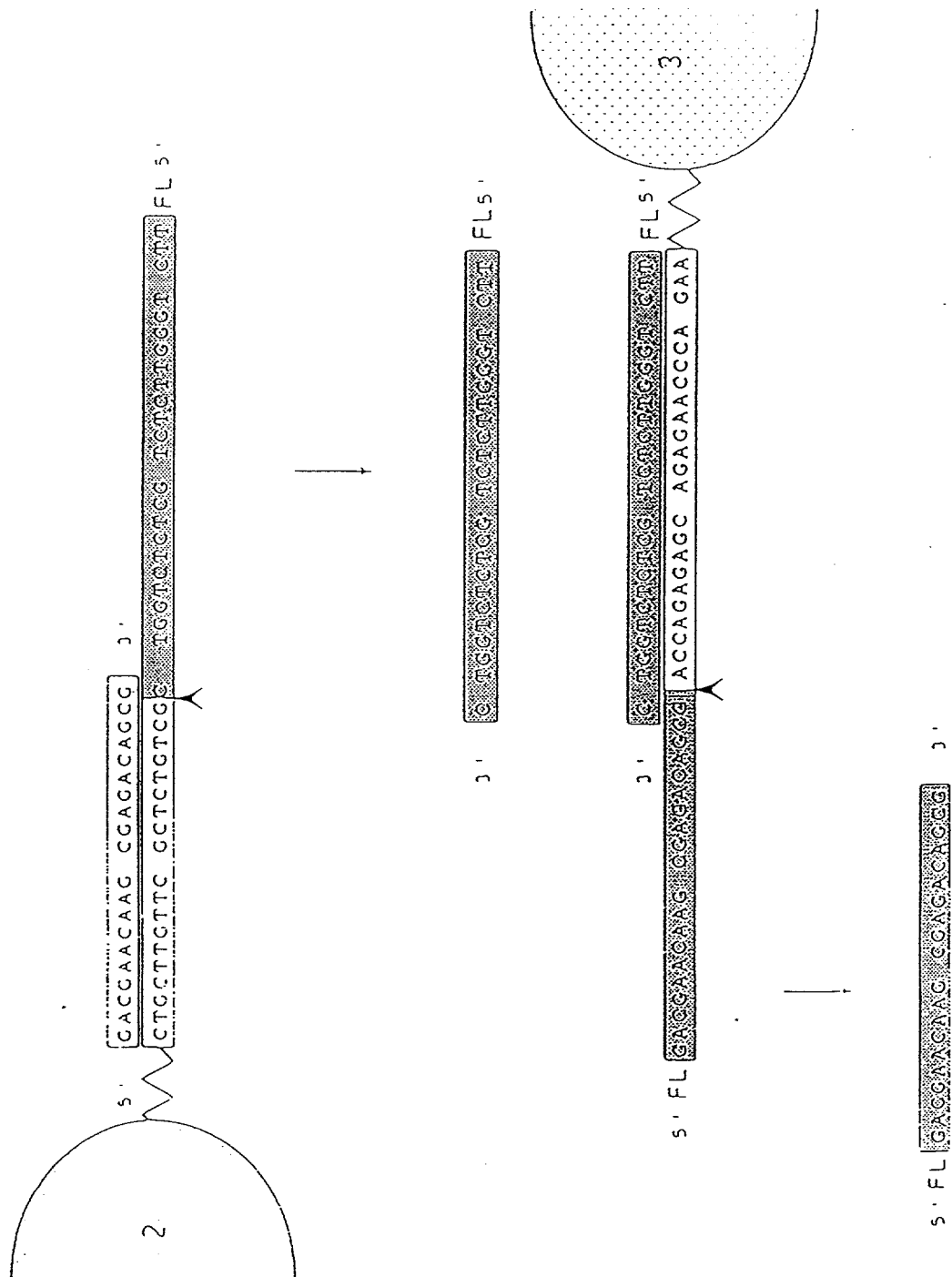
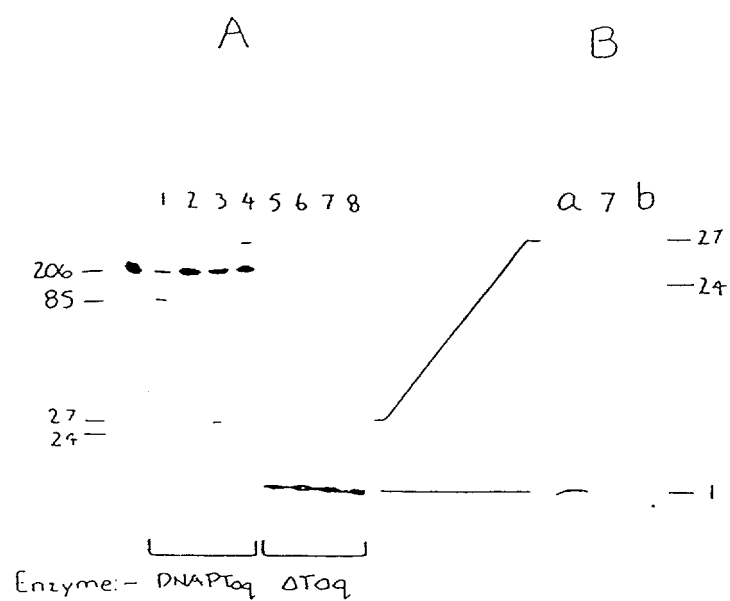


FIGURE 23



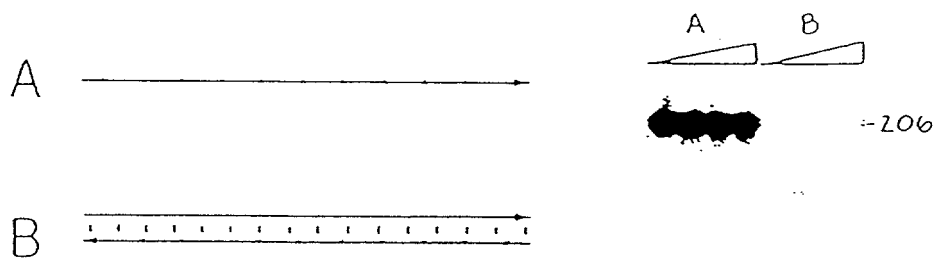
006007 50E48960

FIGURE 25



09684308 100500

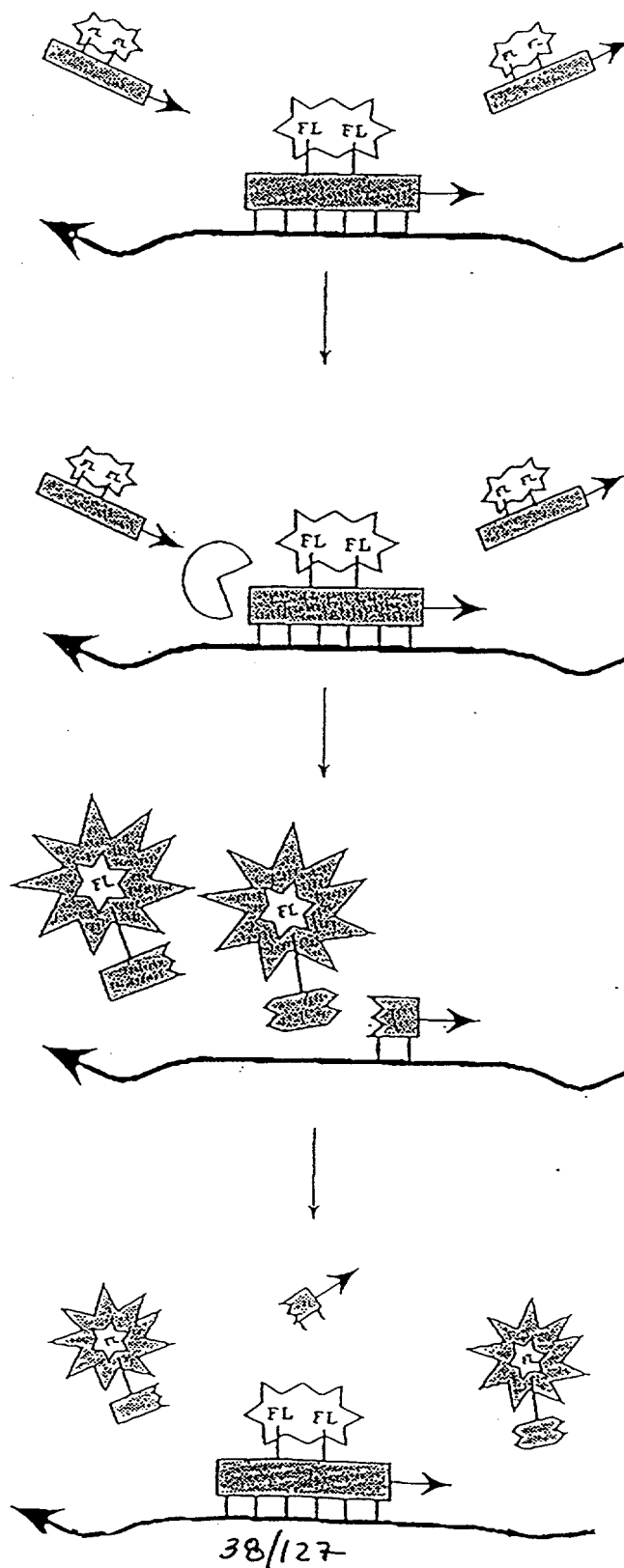
FIGURE 26



$\cdot = {}^{32}\text{P}$

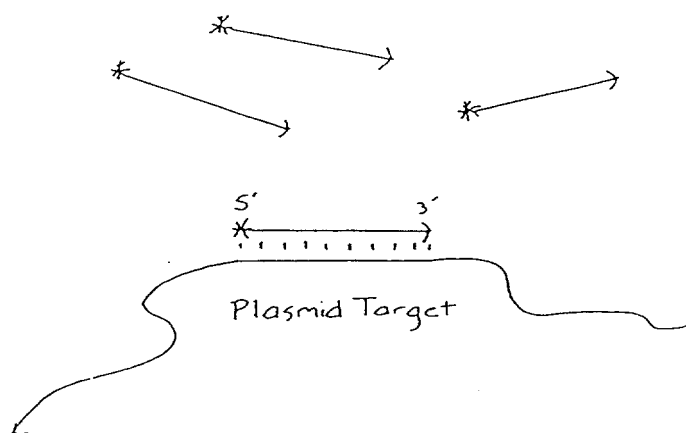
37/127

FIGURE 27



000007 50E42560

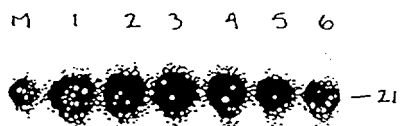
FIGURE 28A



* = ^{32}P 5' terminal phosphate

00684305 10000

FIGURE 28B



-1

FIGURE 29

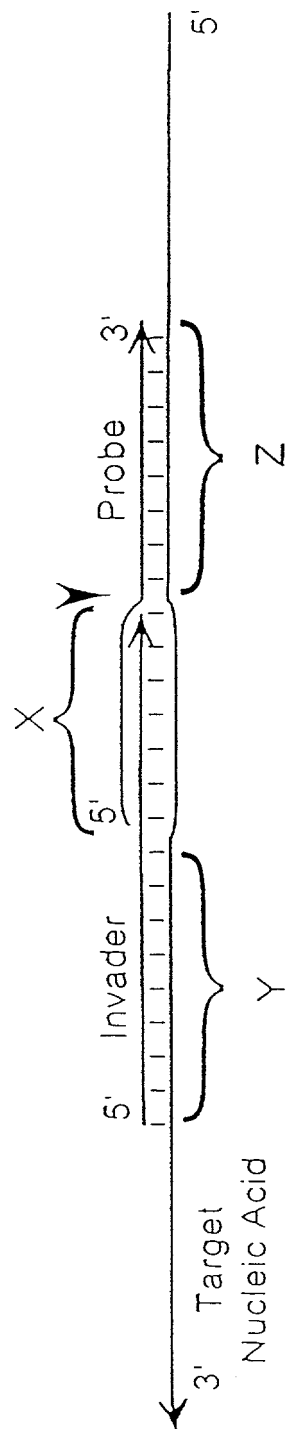


FIGURE 30

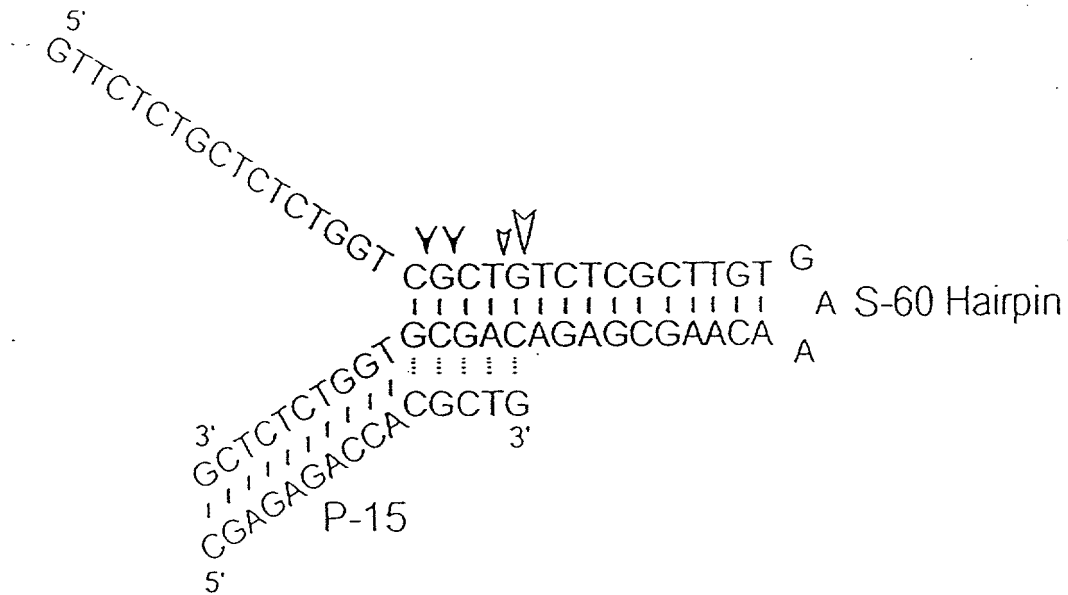


FIGURE 31

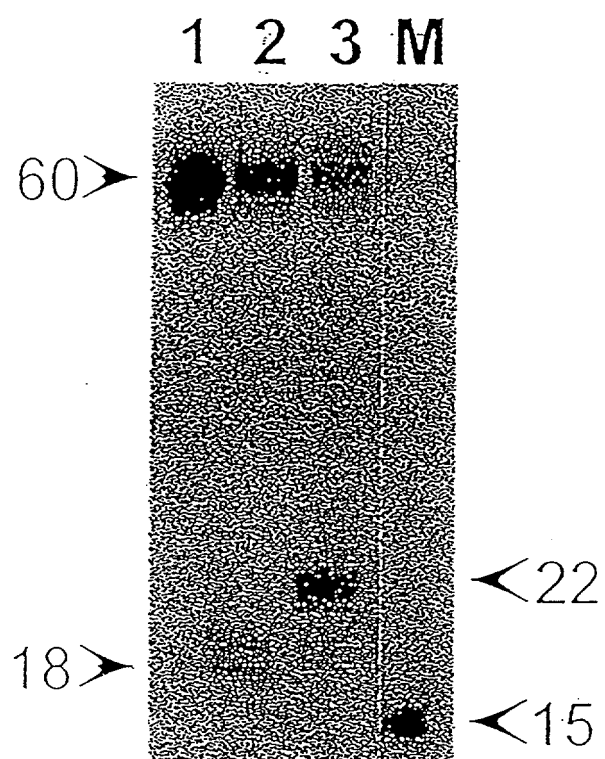
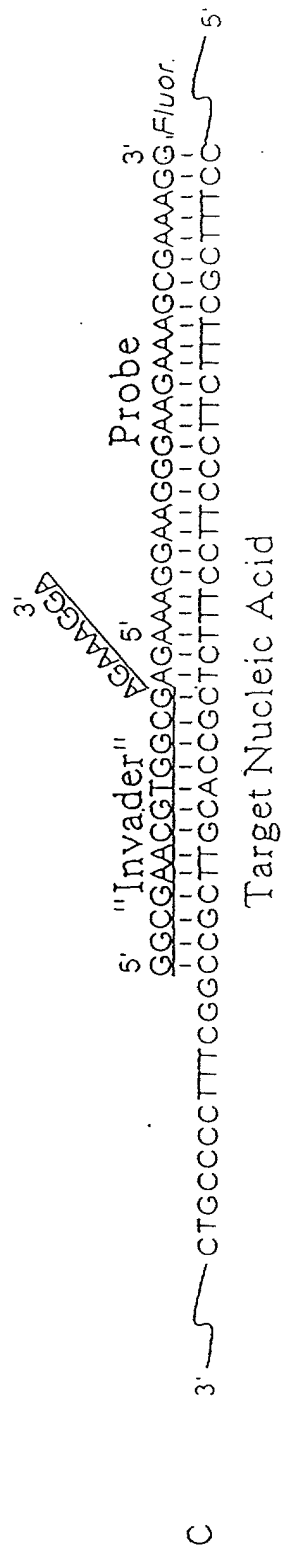
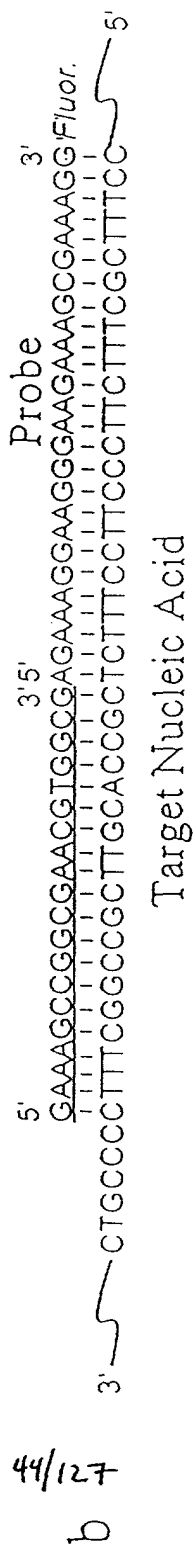
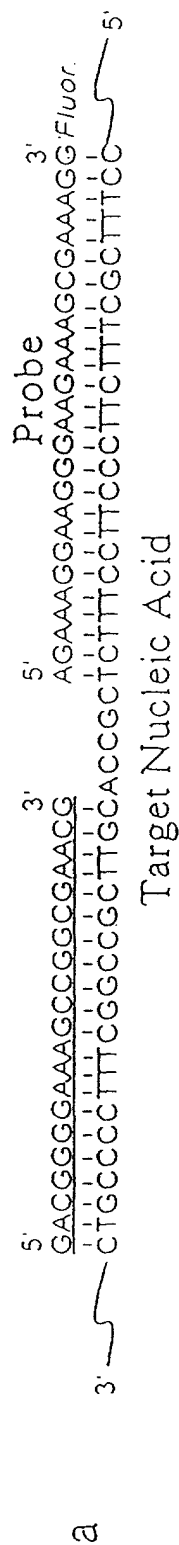


FIGURE 32



00900T" SDE+8960

8

7

6

5

4

3

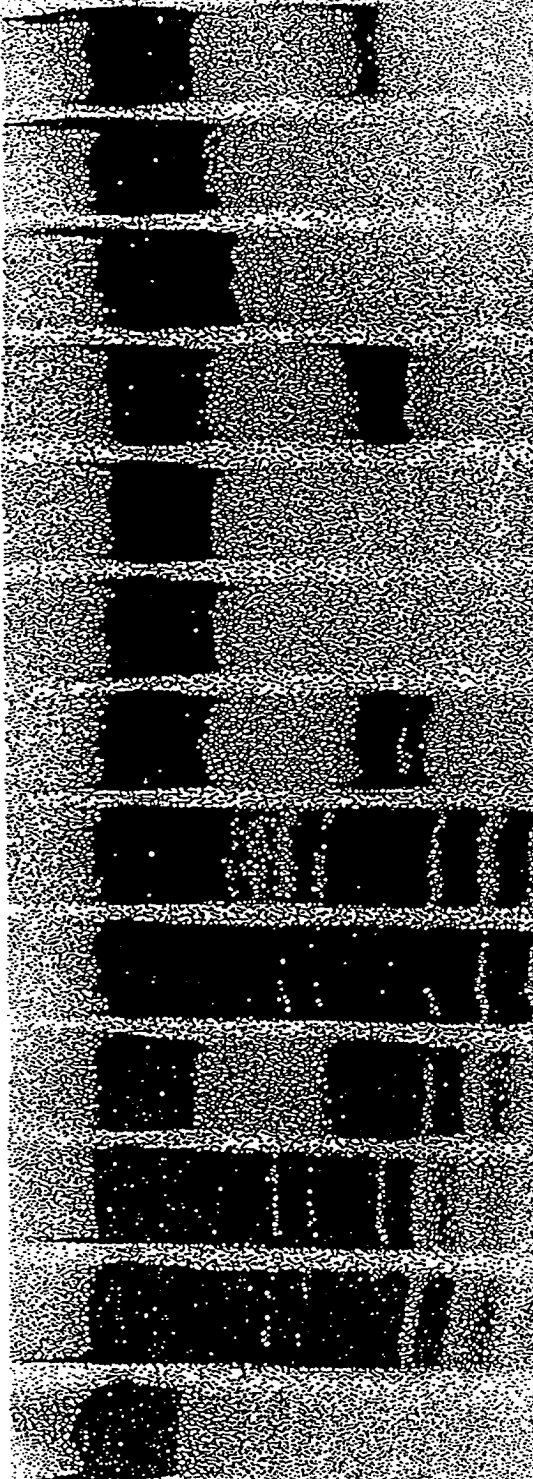
2

1

45/127

FIGURE 34 50E+18960

M 1 2 3 4 5 6 7 8 9 10 11 12



A

46/127

FIGURE 55 DEC 78 95D

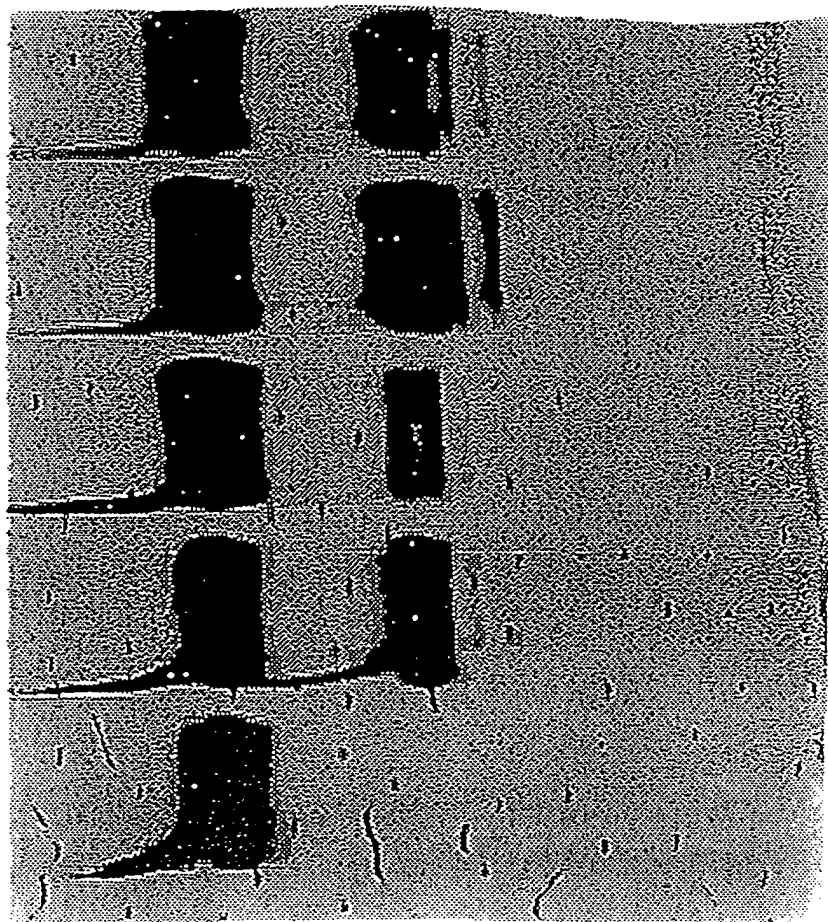
5

4

3

2

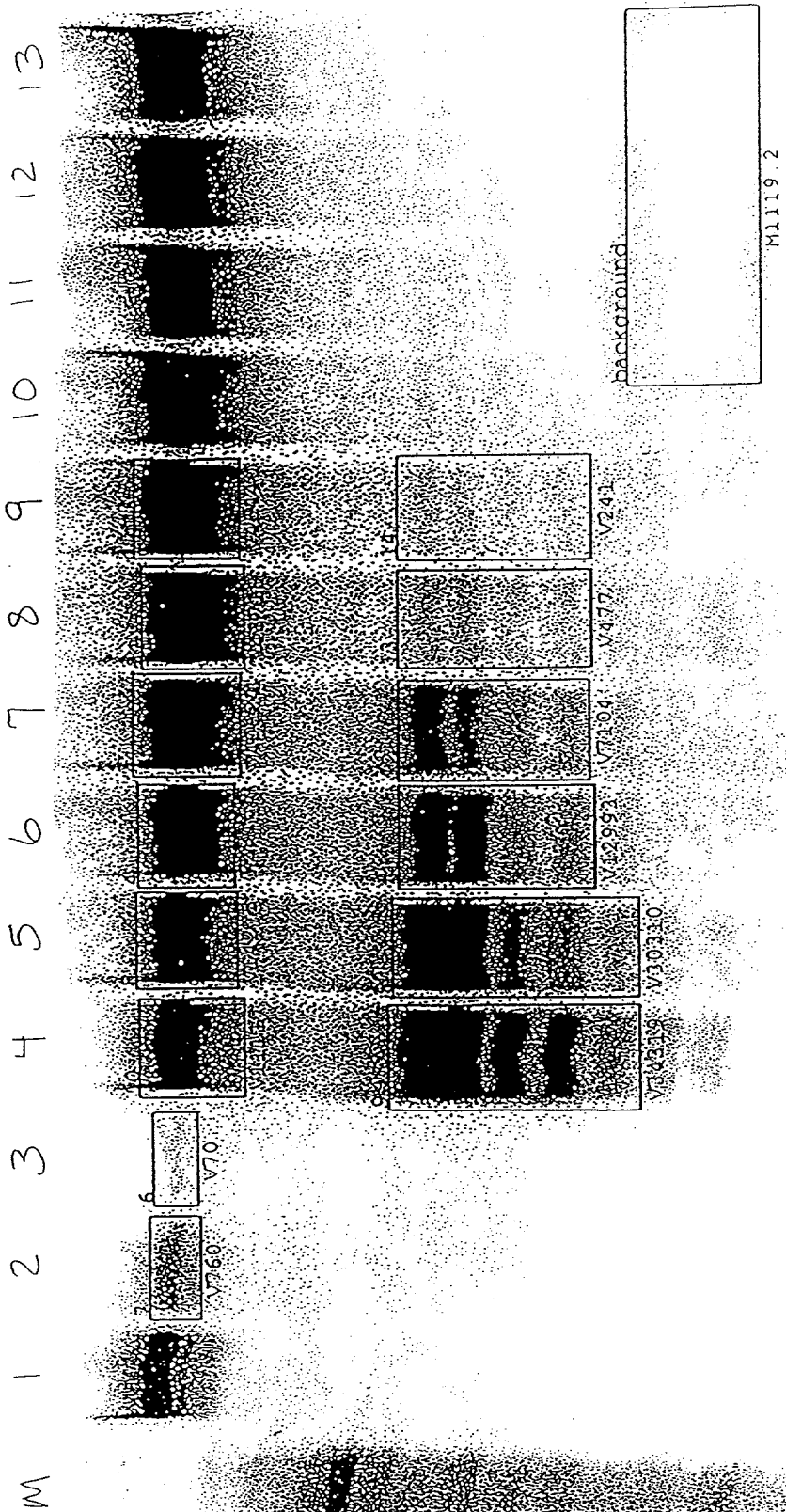
1



26
A

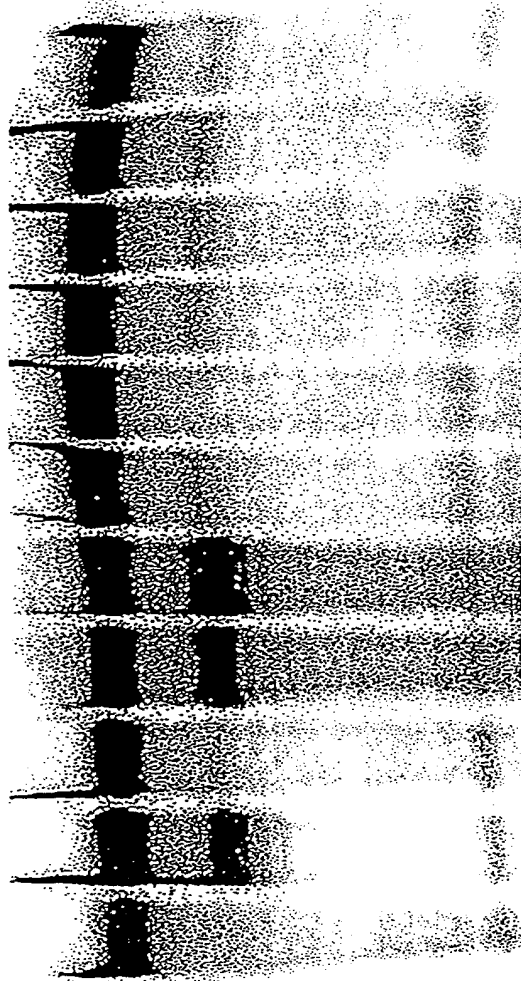
47/127

FIGURE 36



00371E48960

1 2 3 4 5 6 7 8 9 10 11



A A

49/127

00900T" 50678960

FIGURE 38

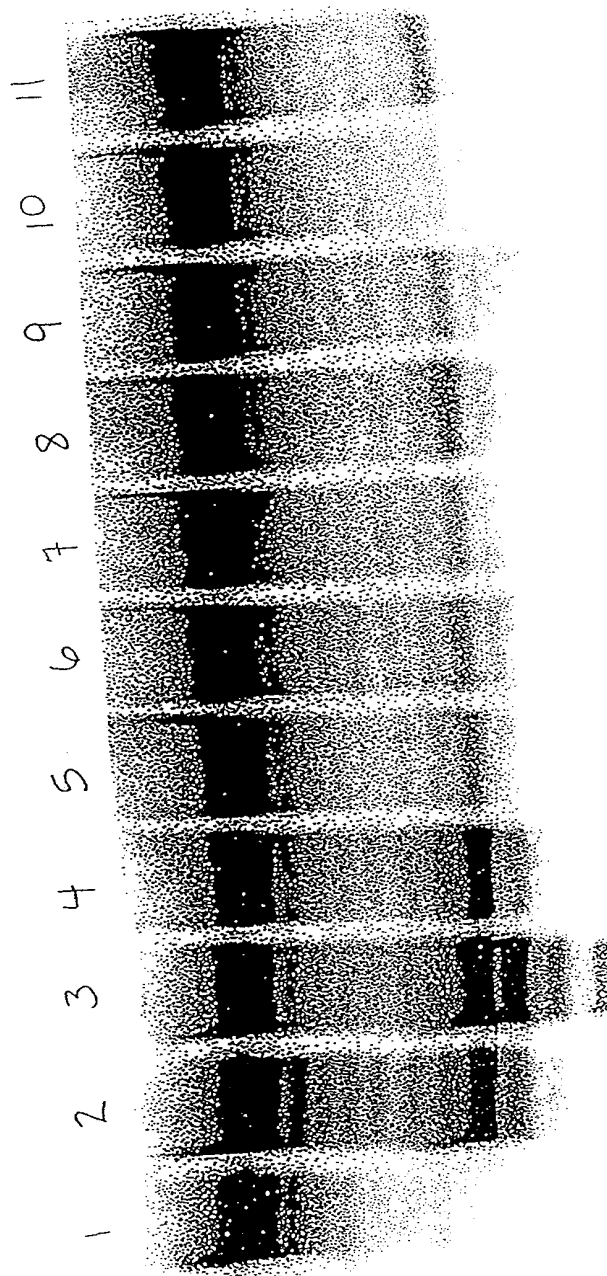


FIGURE 39

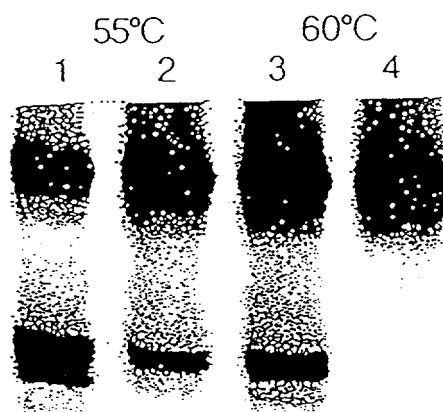
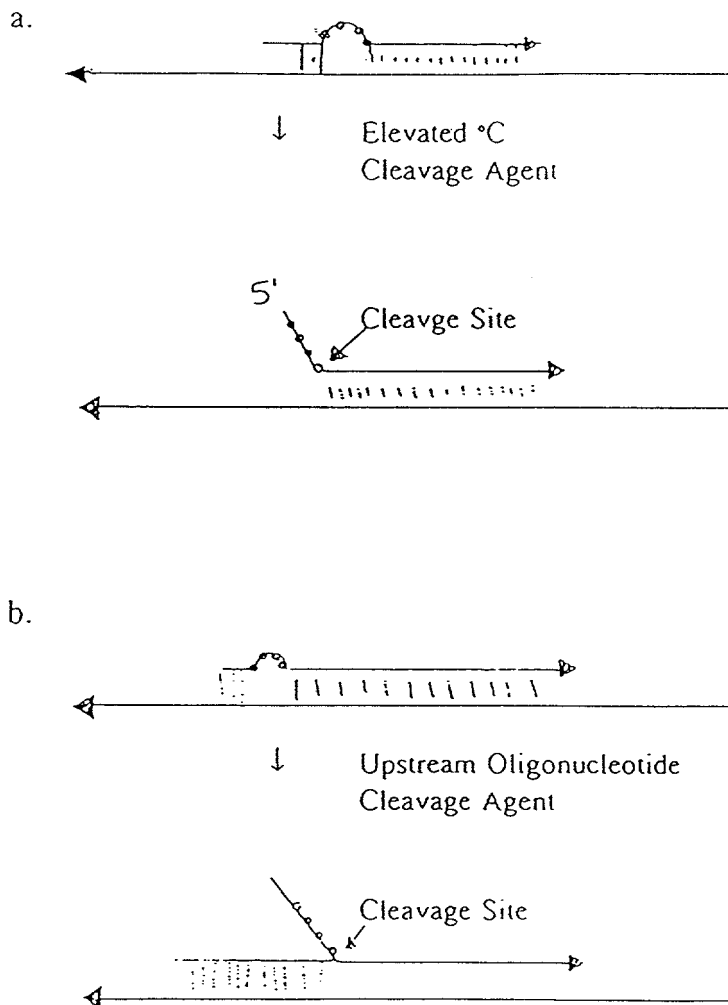


FIGURE 40



009007" 50E+8960

FIGURE 41

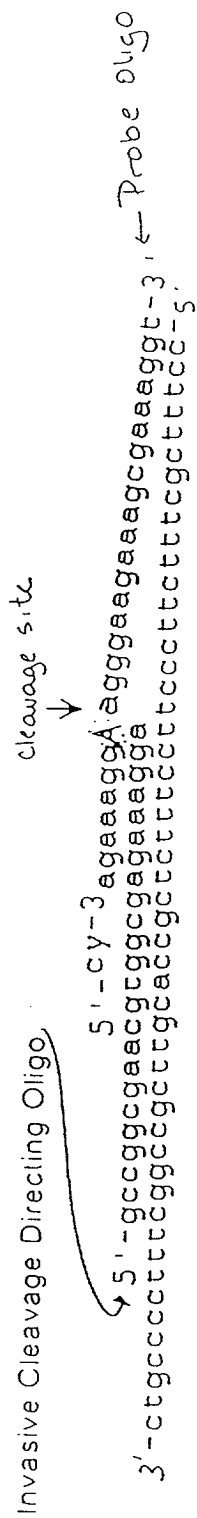
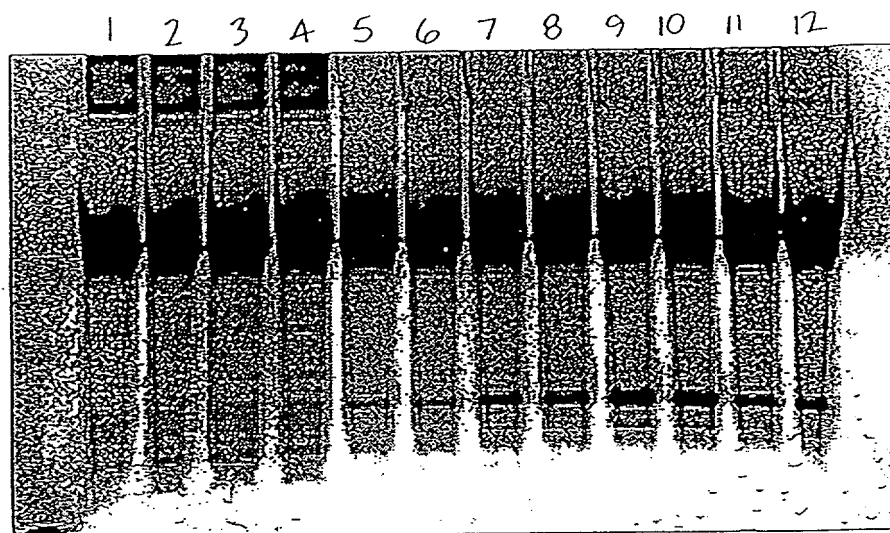
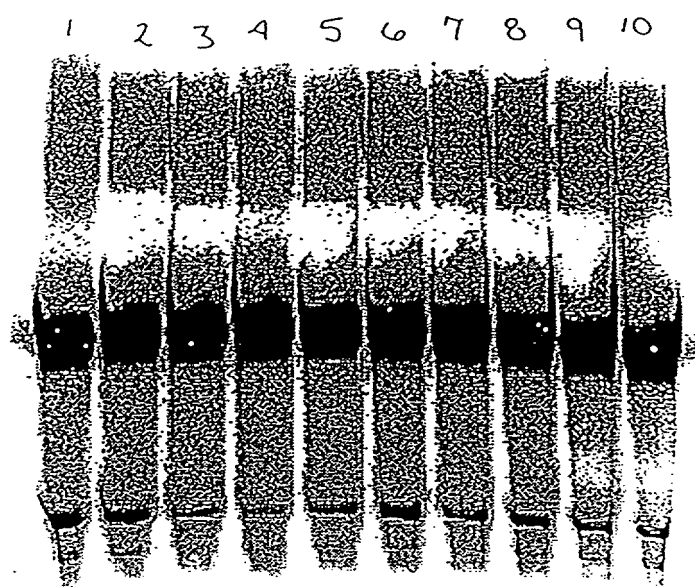


FIGURE 42



009007-50E+2560

FIGURE 43



009007-50E+8960

FIGURE 44

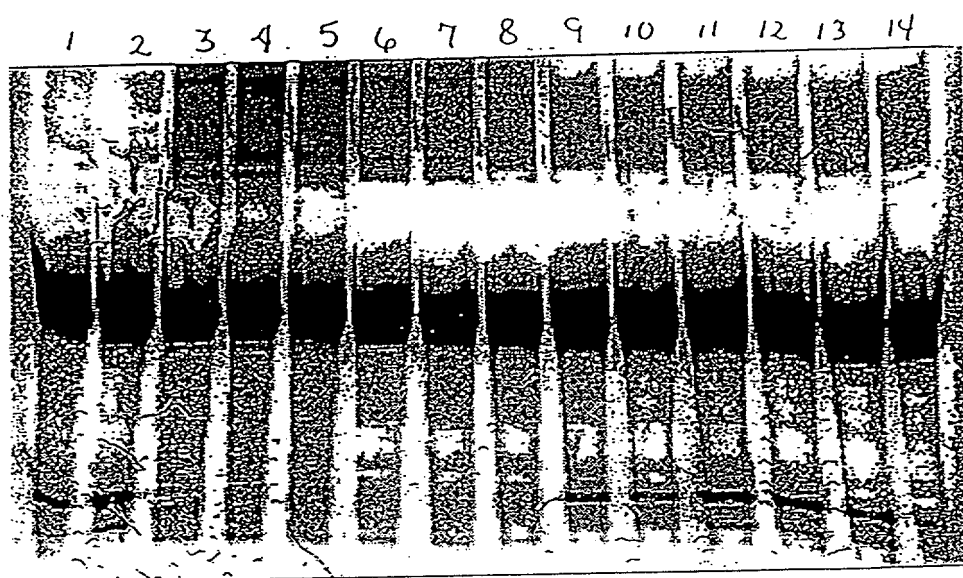
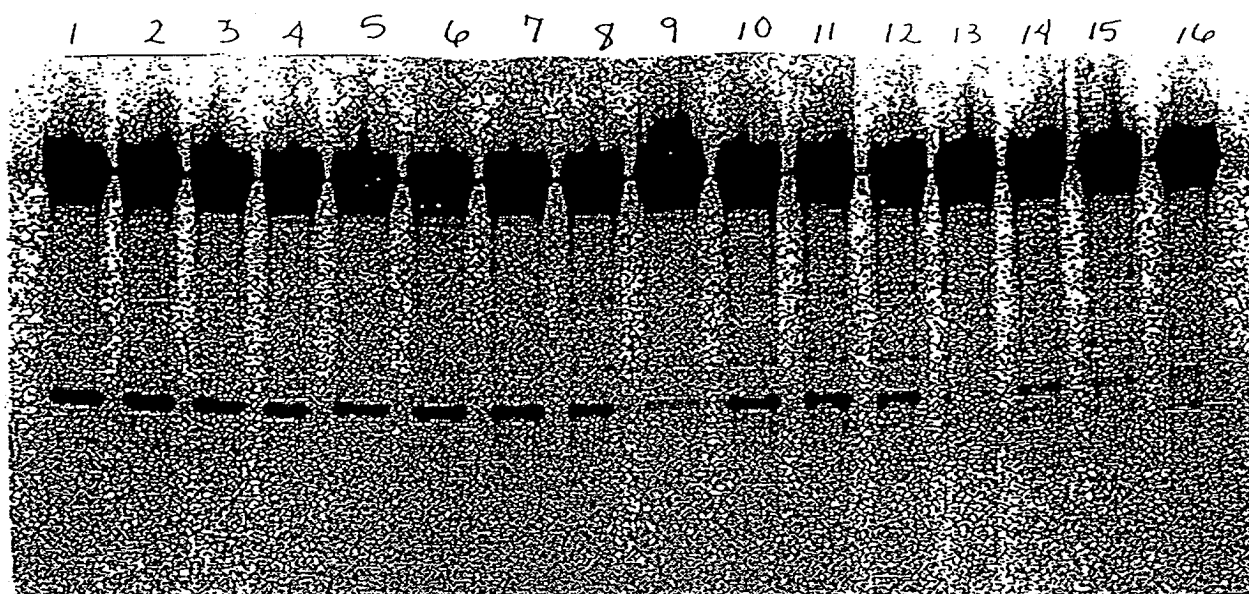
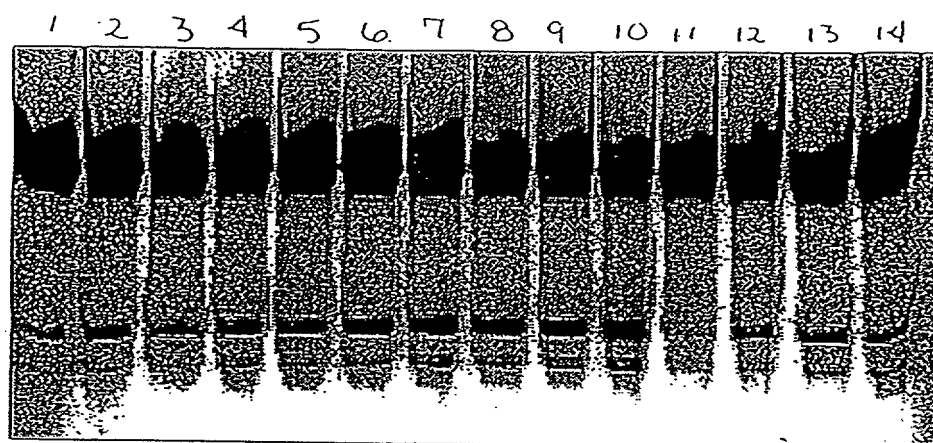


FIGURE 45



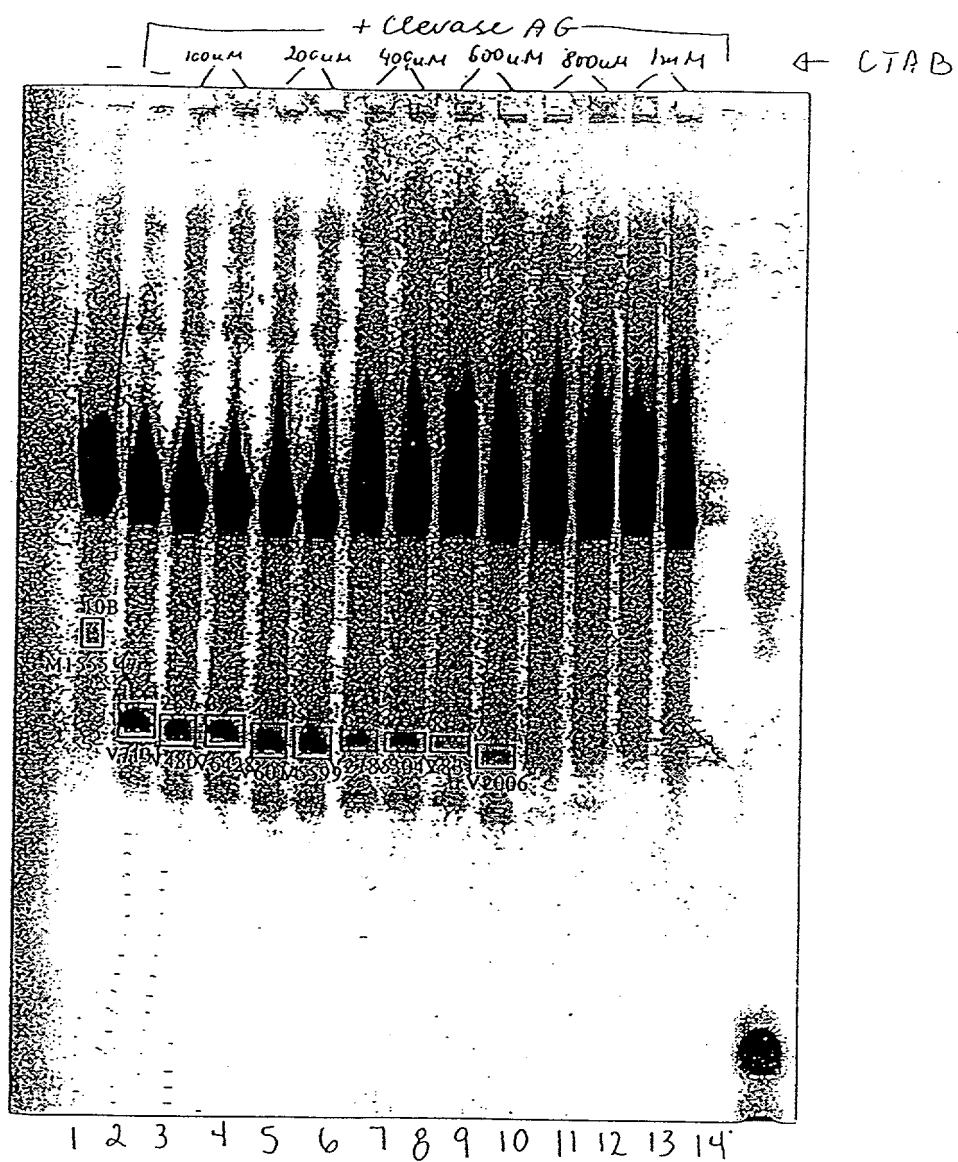
009807" 50348960

FIGURE 46



009007 50E+8560

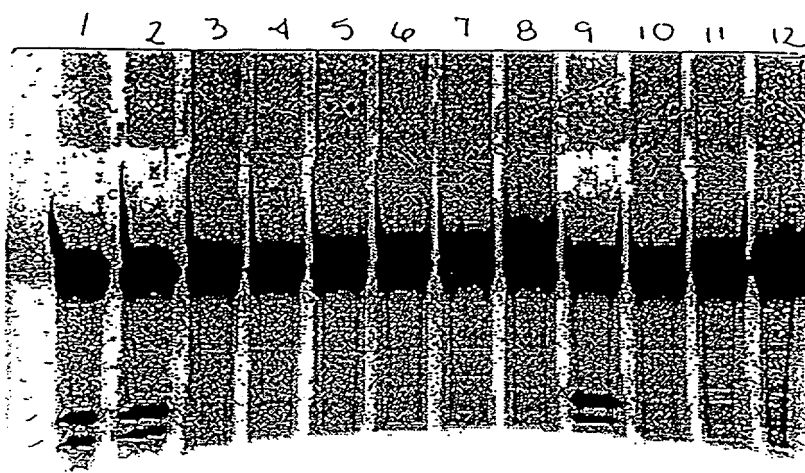
FIGURE 47



59/127

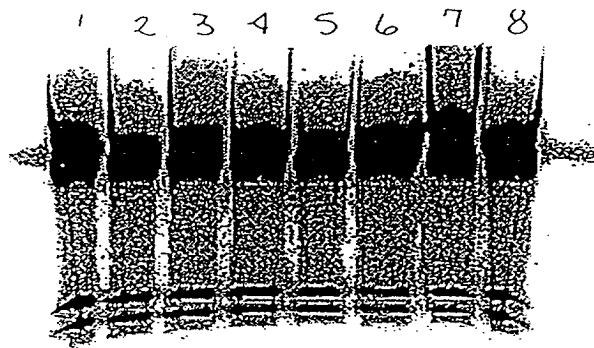
09684305 100600

FIGURE 48



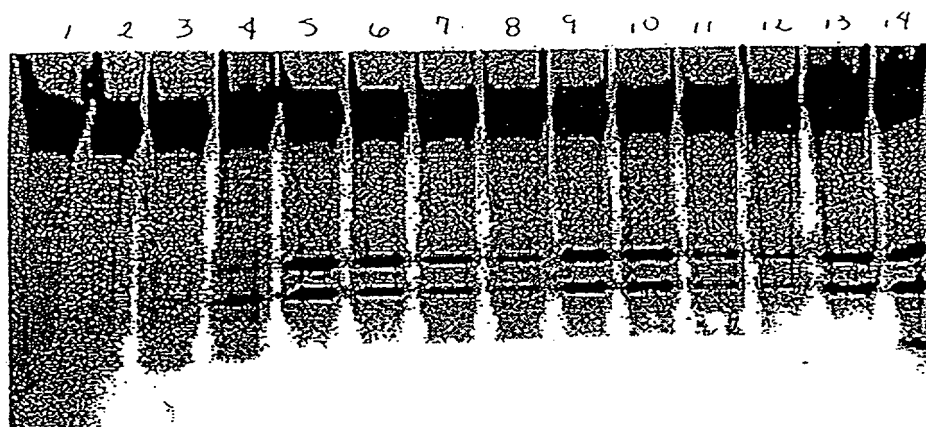
60/127

FIGURE 49



09684305 100600

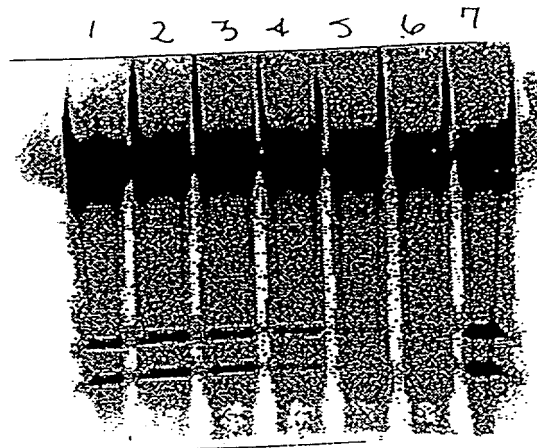
FIGURE 50



09684305 100600

62/127

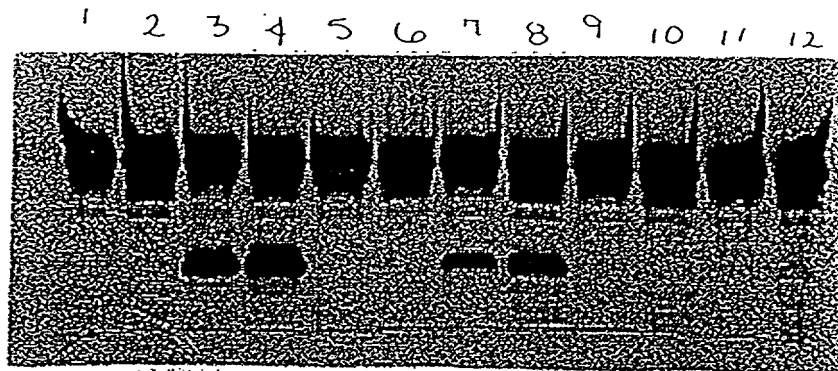
FIGURE 51



00500T" 50E48960

63/127

FIGURE 52



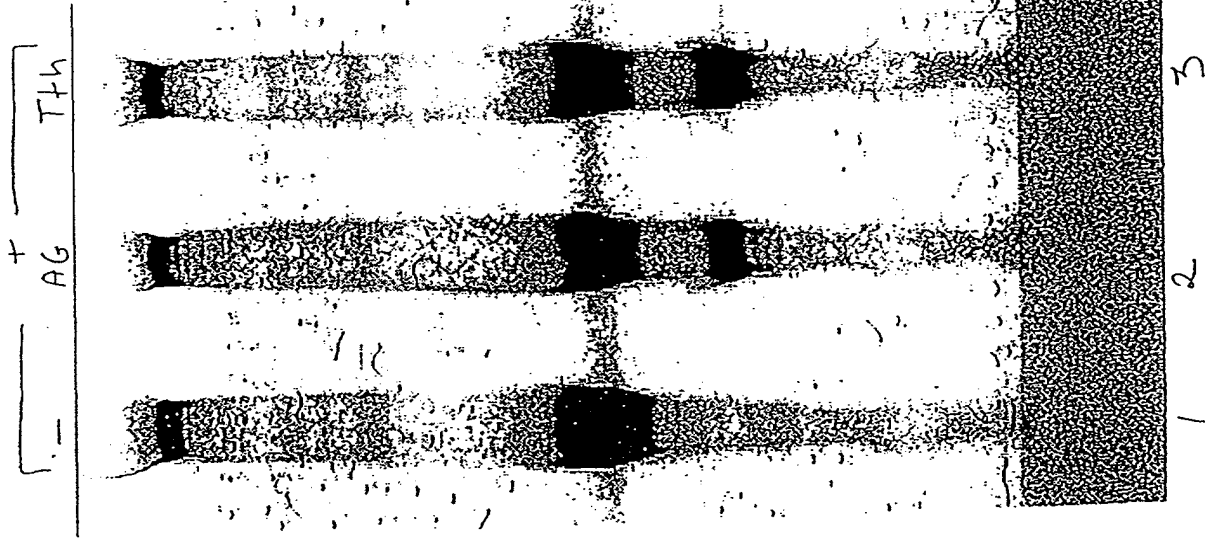
09684305-100600

64/127

009007" 50E49960

FIGURE 53

a



TARGET RWA

UNCLEAVED
PROSE

CLEAVED
PROSE

65/127

b

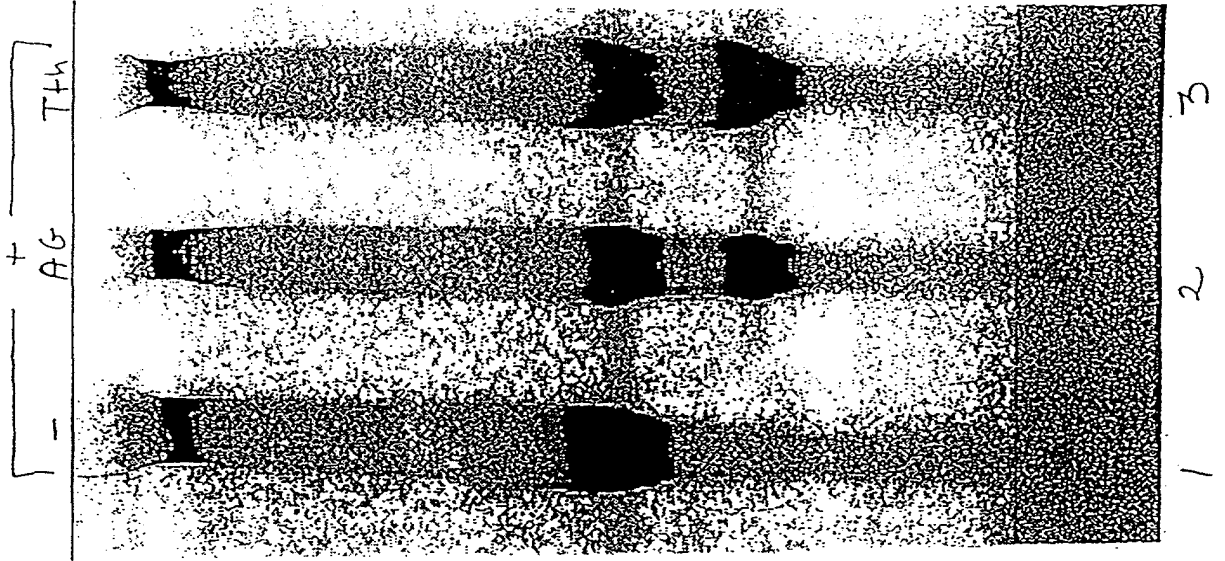
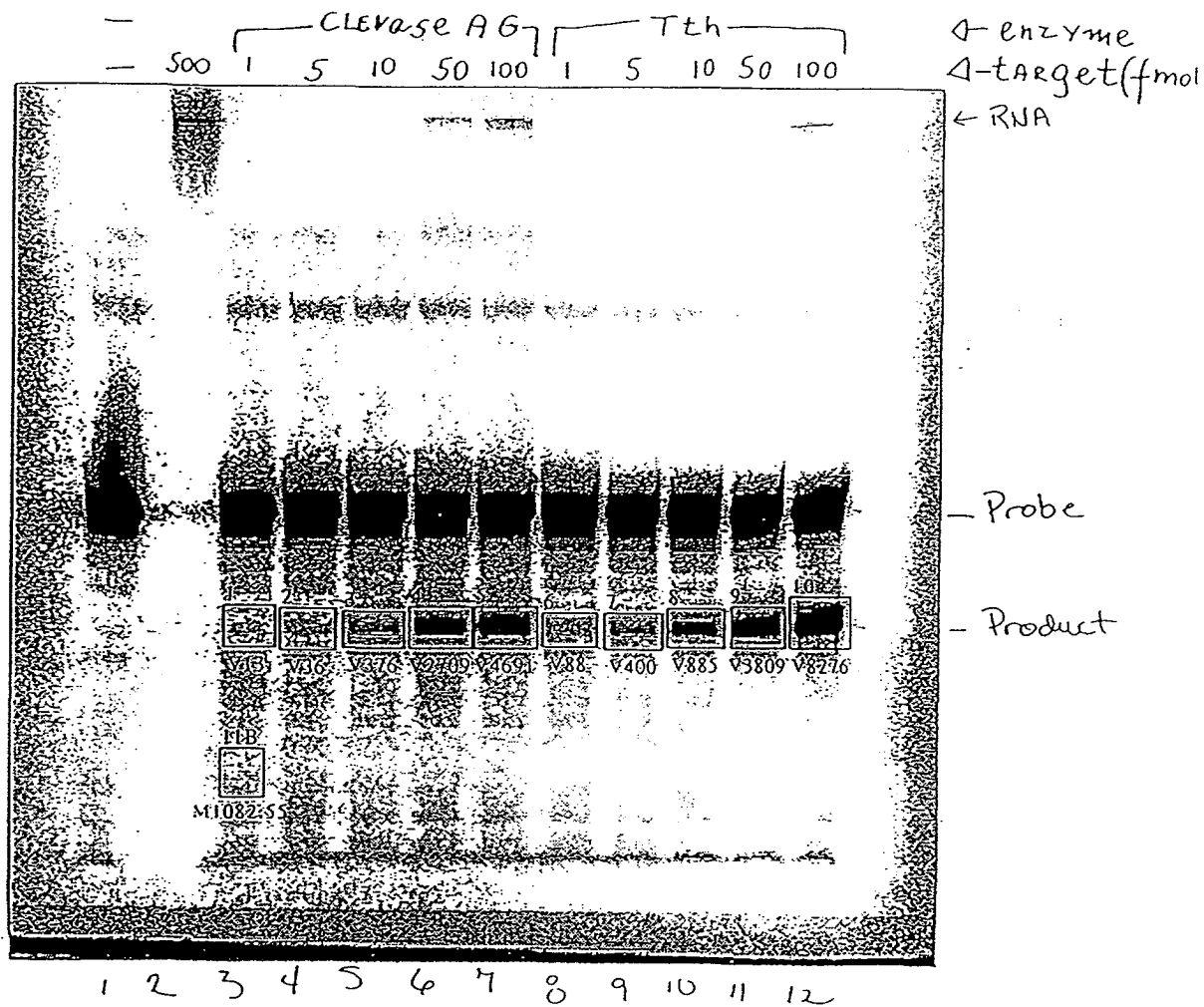
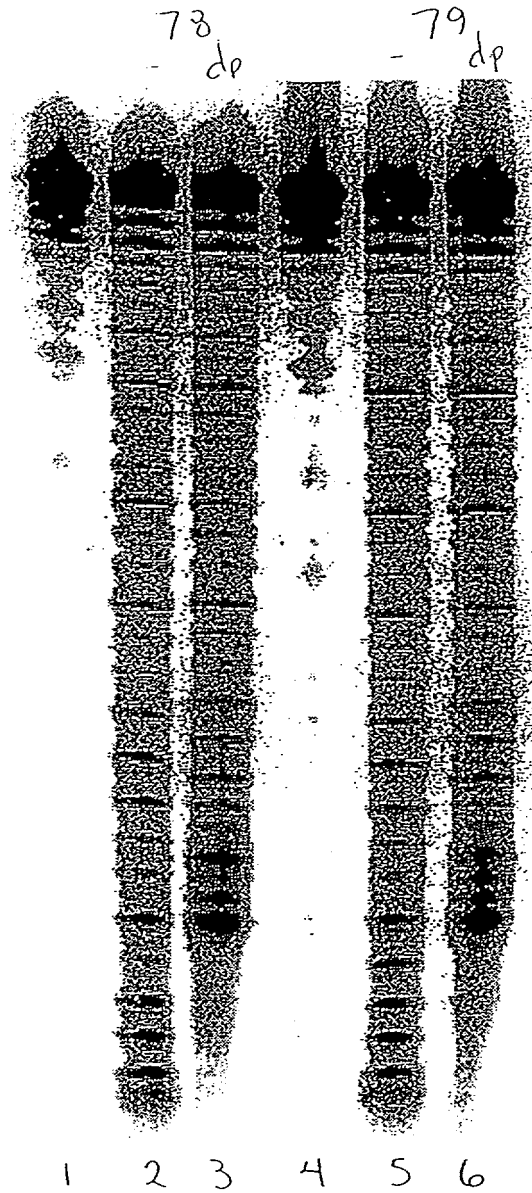


FIGURE 54



66/127

FIGURE 55



009007-50E48960

FIGURE 56

70 (C10 aminoT's)
74 (C6 amino T's)

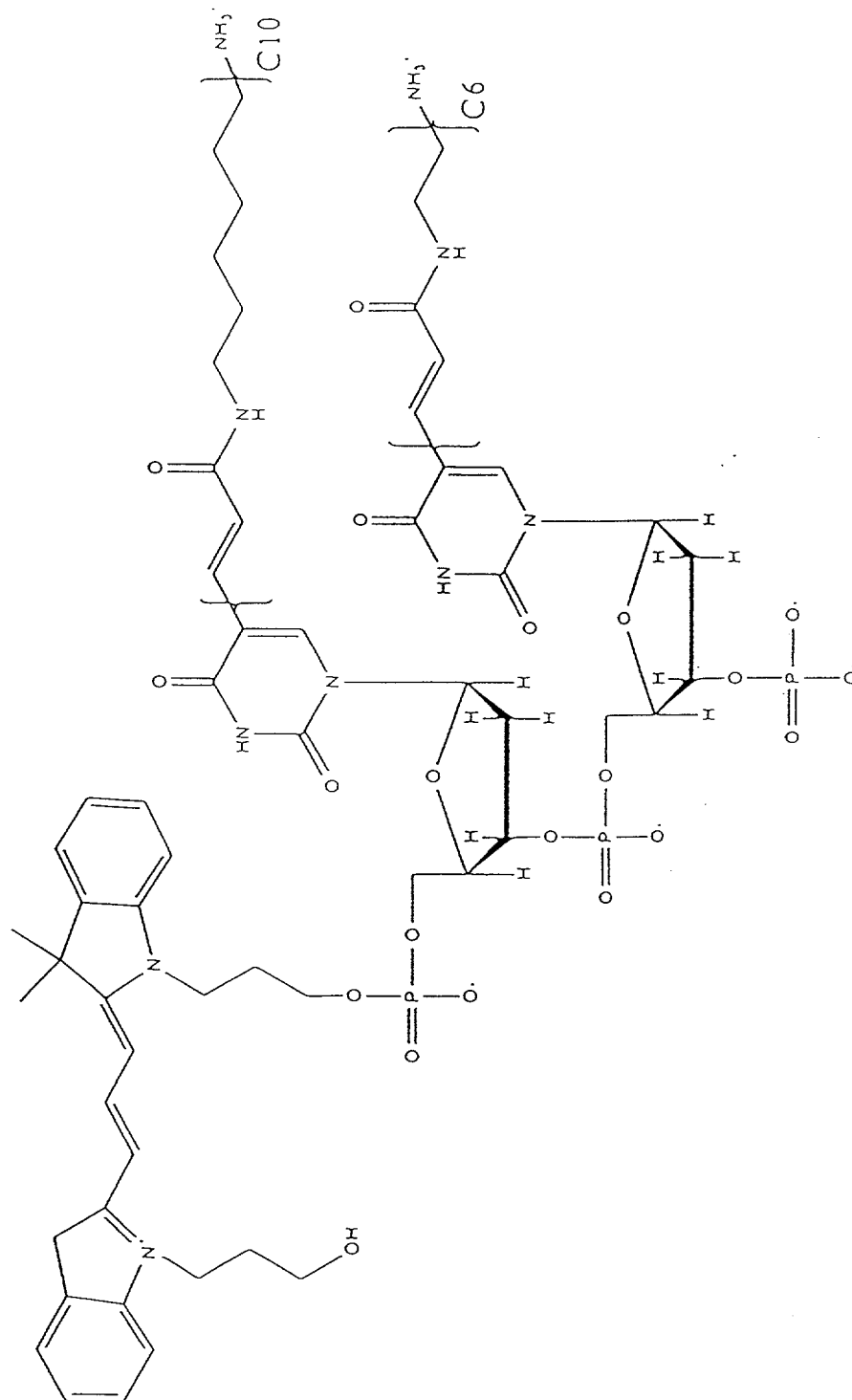
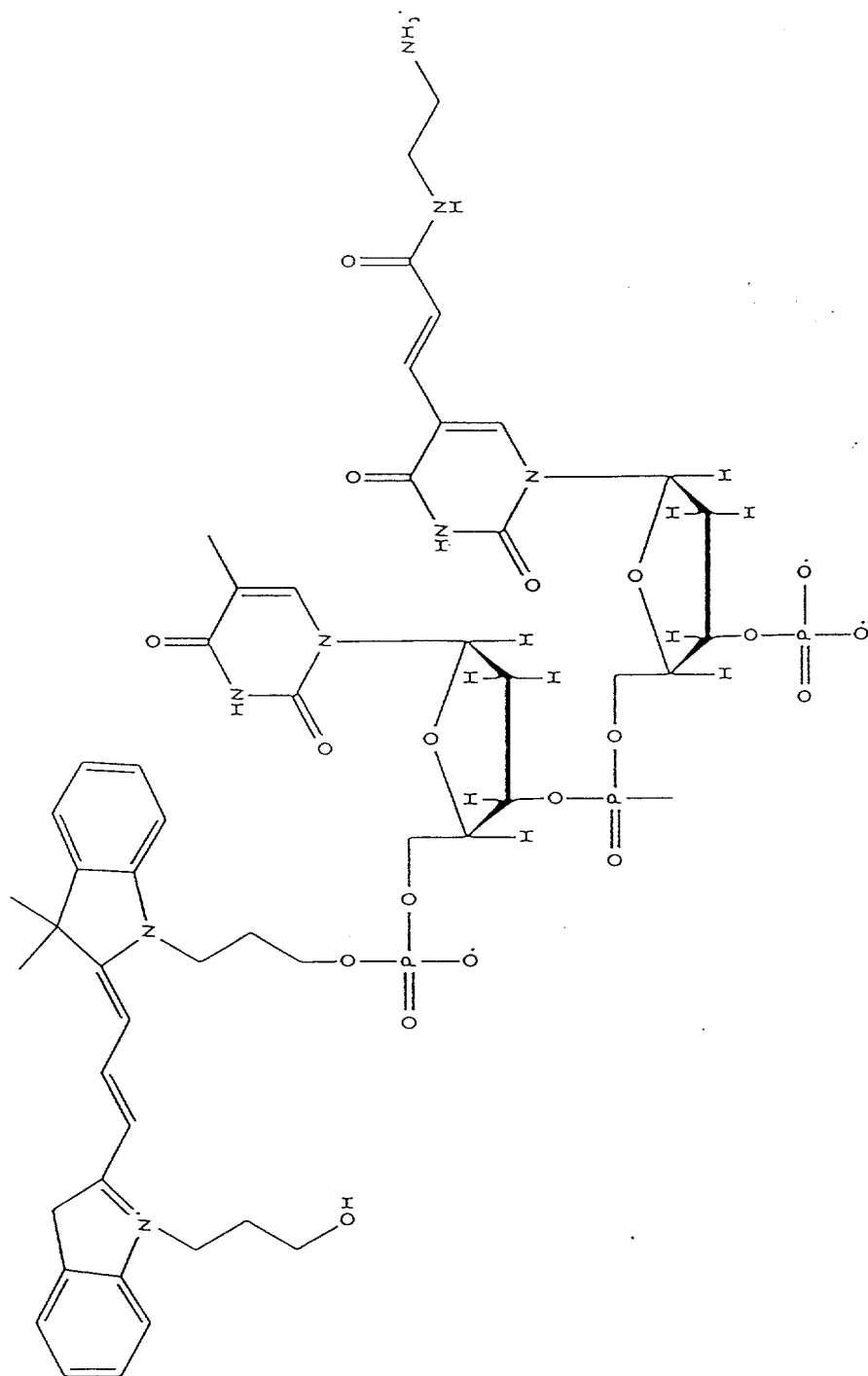


FIGURE 57

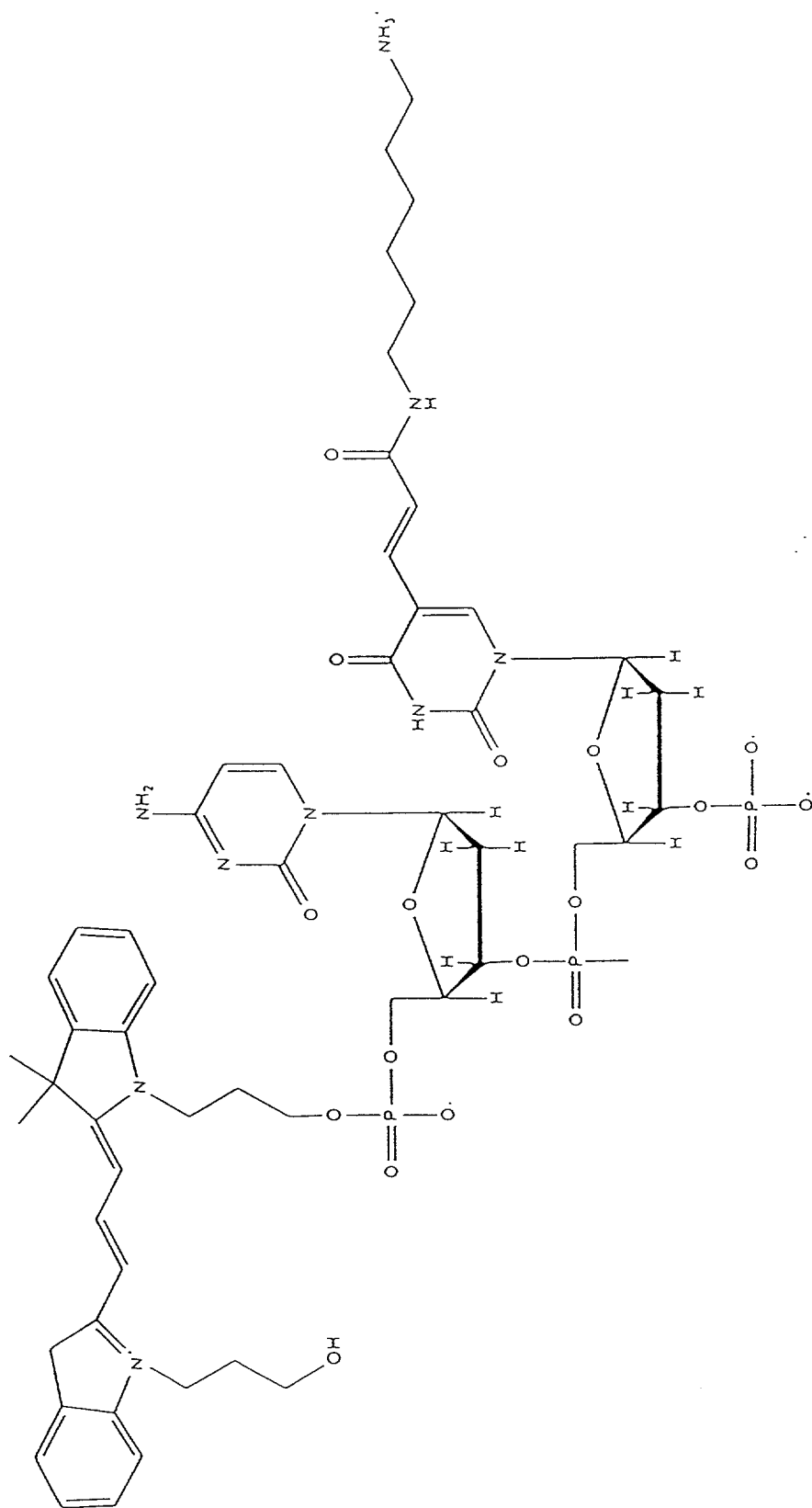
75



69/127

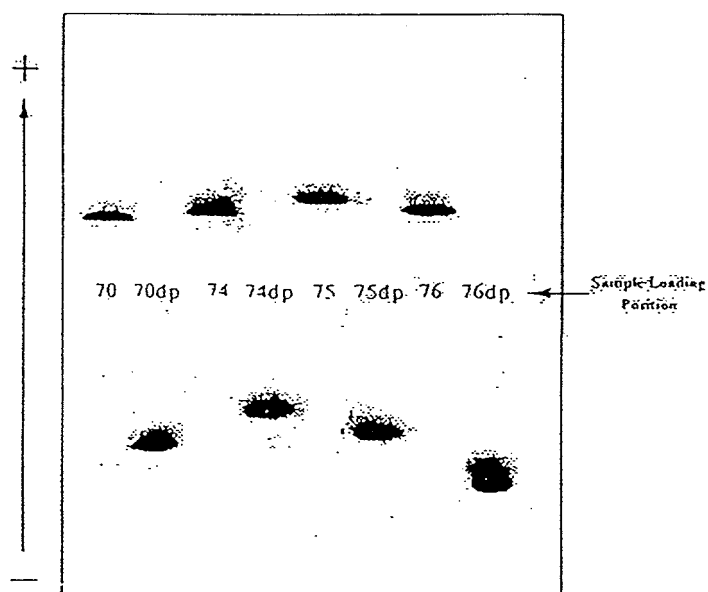
FIGURE 58

76



70/127

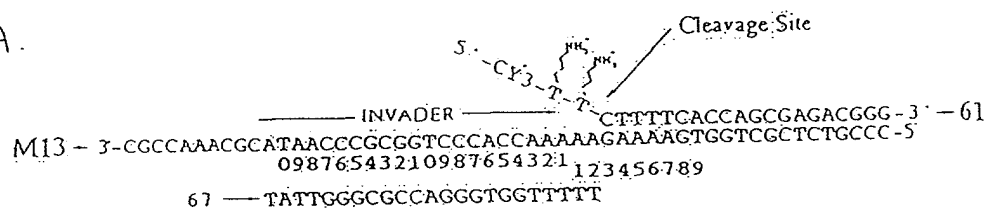
FIGURE 59



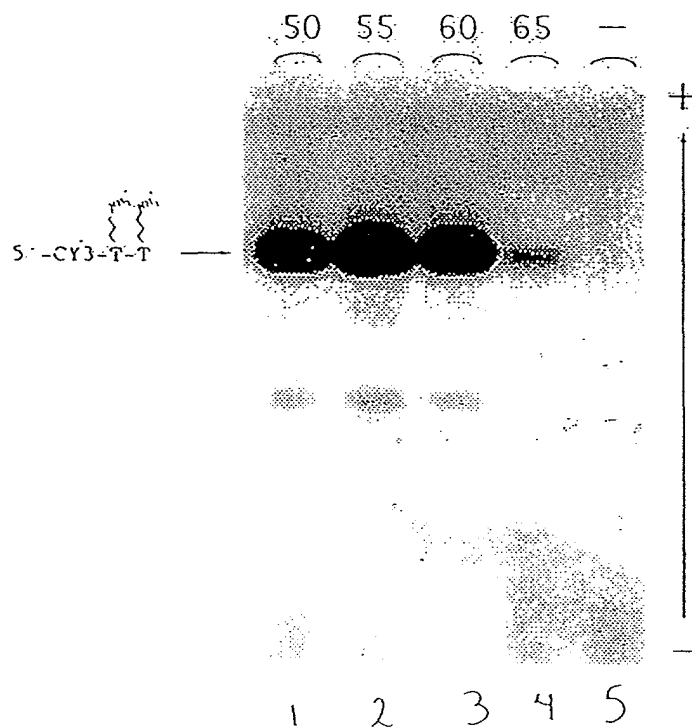
71/127

FIGURE 60

A.

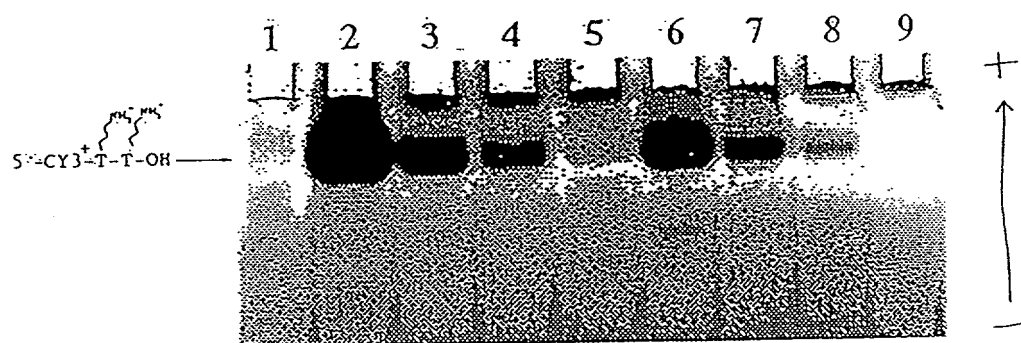


B.



72/127

FIGURE 61



73/127

09684305-100500

FIGURE 62

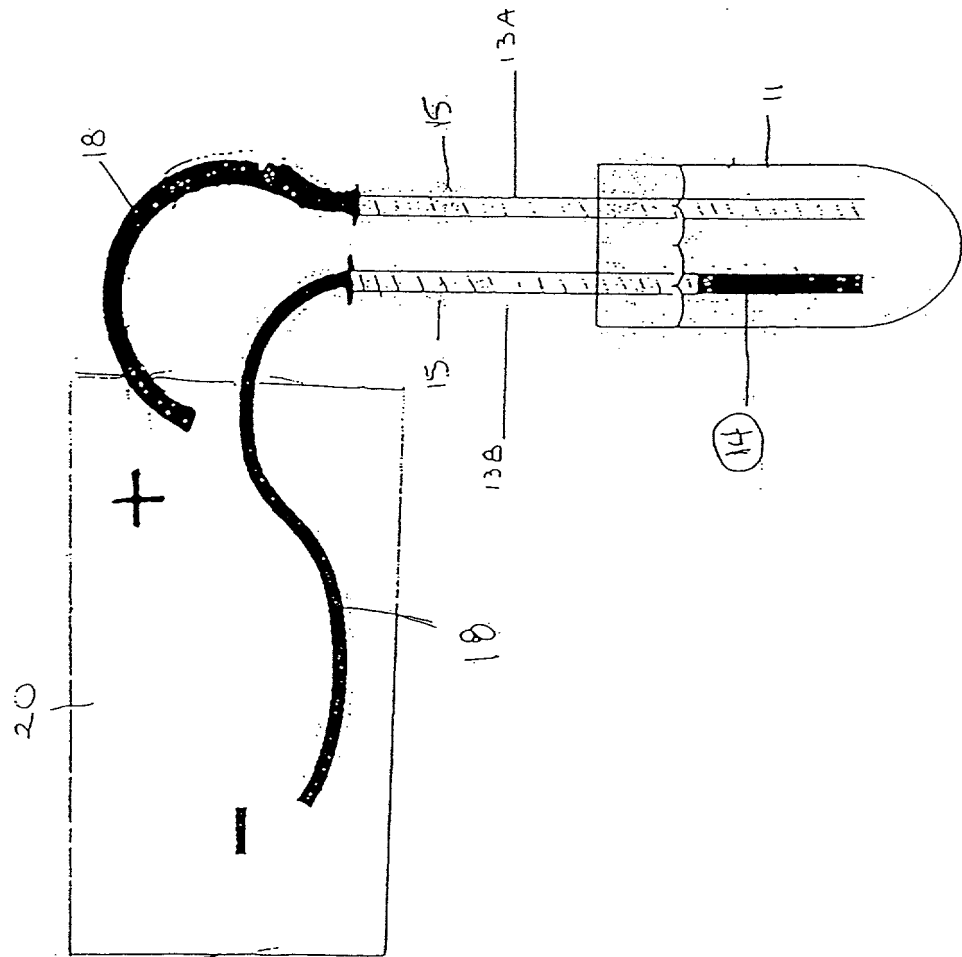
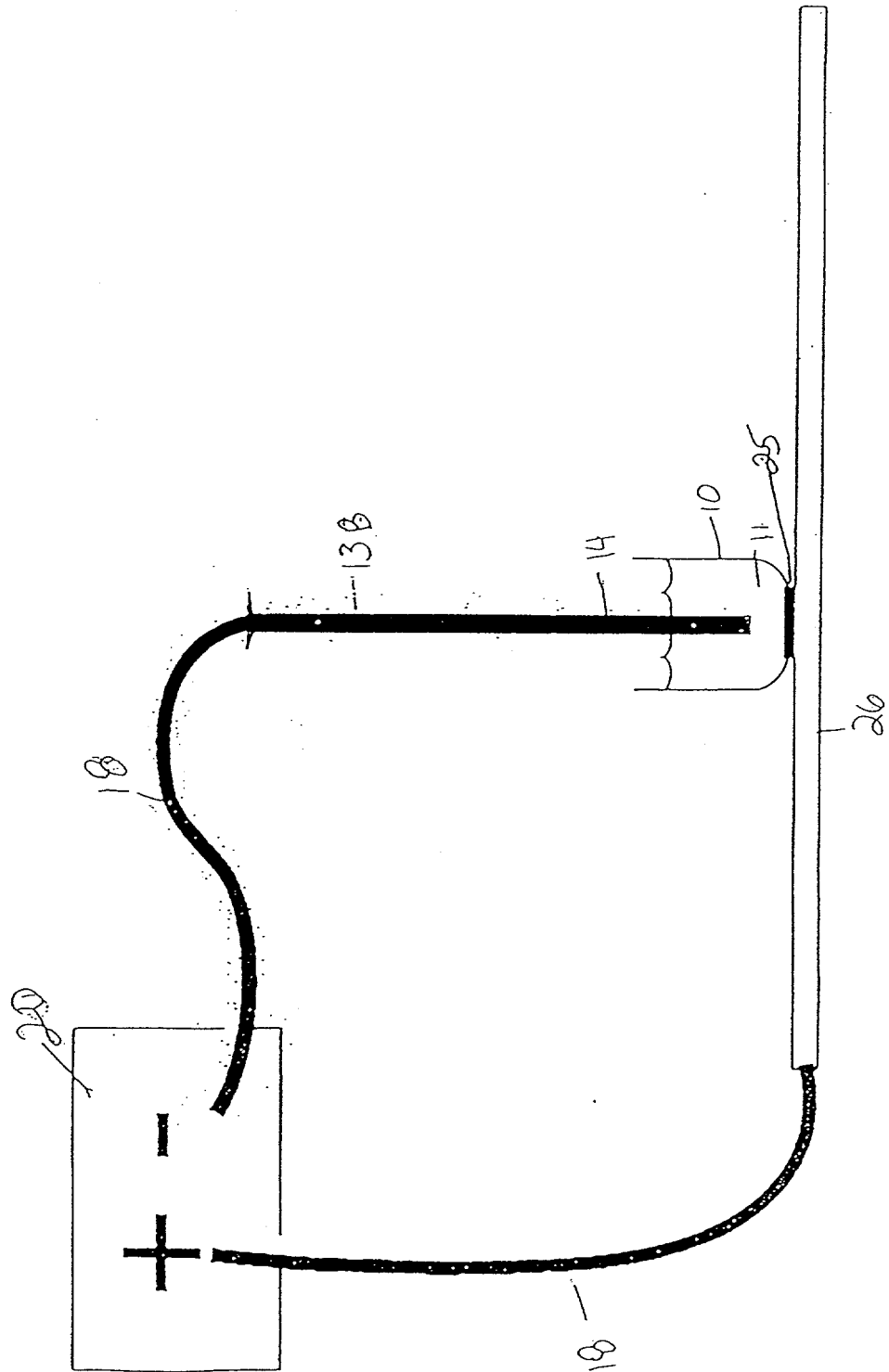


FIGURE 63



00684305-100600

FIGURE 64

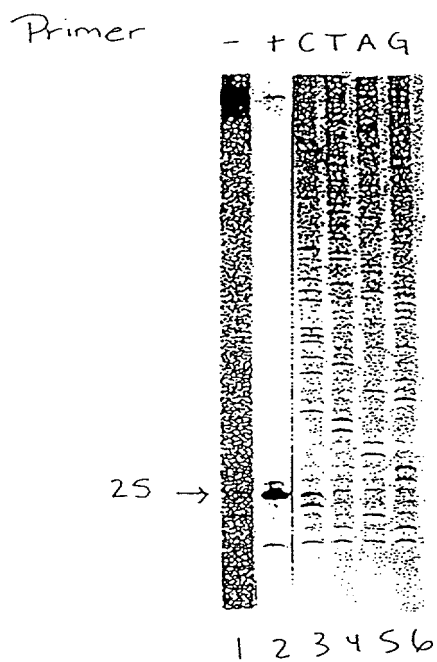
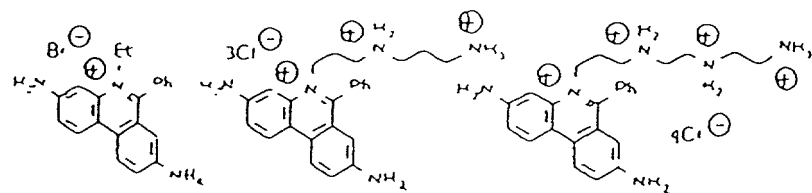




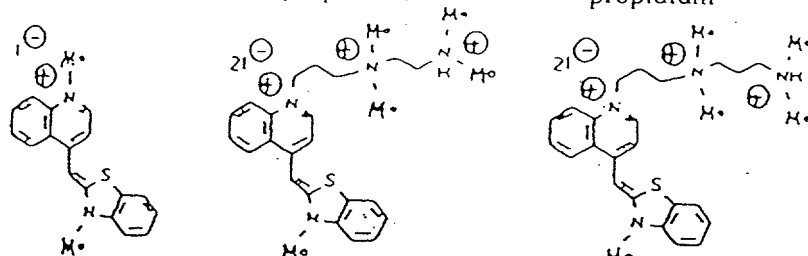
FIGURE 65



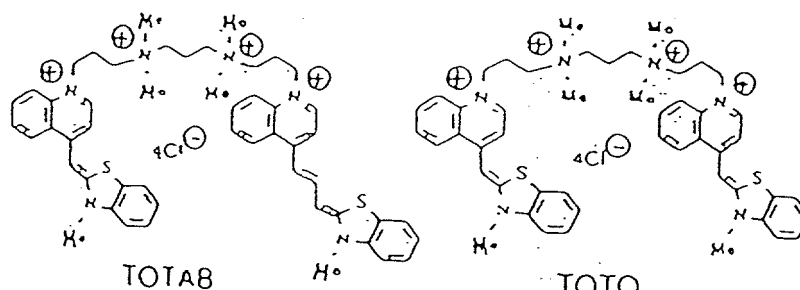
FIGURE 66



Ethidium Bromide (1,3-propanediamino)-propidium (diethylenetriamino)-propidium

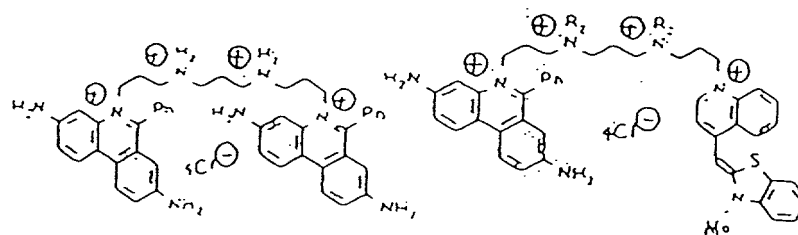


Thiazole Orange (N,N'-tetramethyl-1,2-ethanediamino)-propyl thiazole orange (N,N'-tetramethyl-1,3-propanediamino)-propyl thiazole orange



TOTAB

TOTO



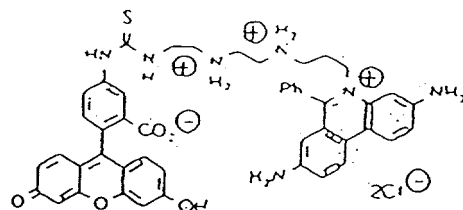
EtH0

TOED1

TOED2

(R = H)

(R = CH₃)

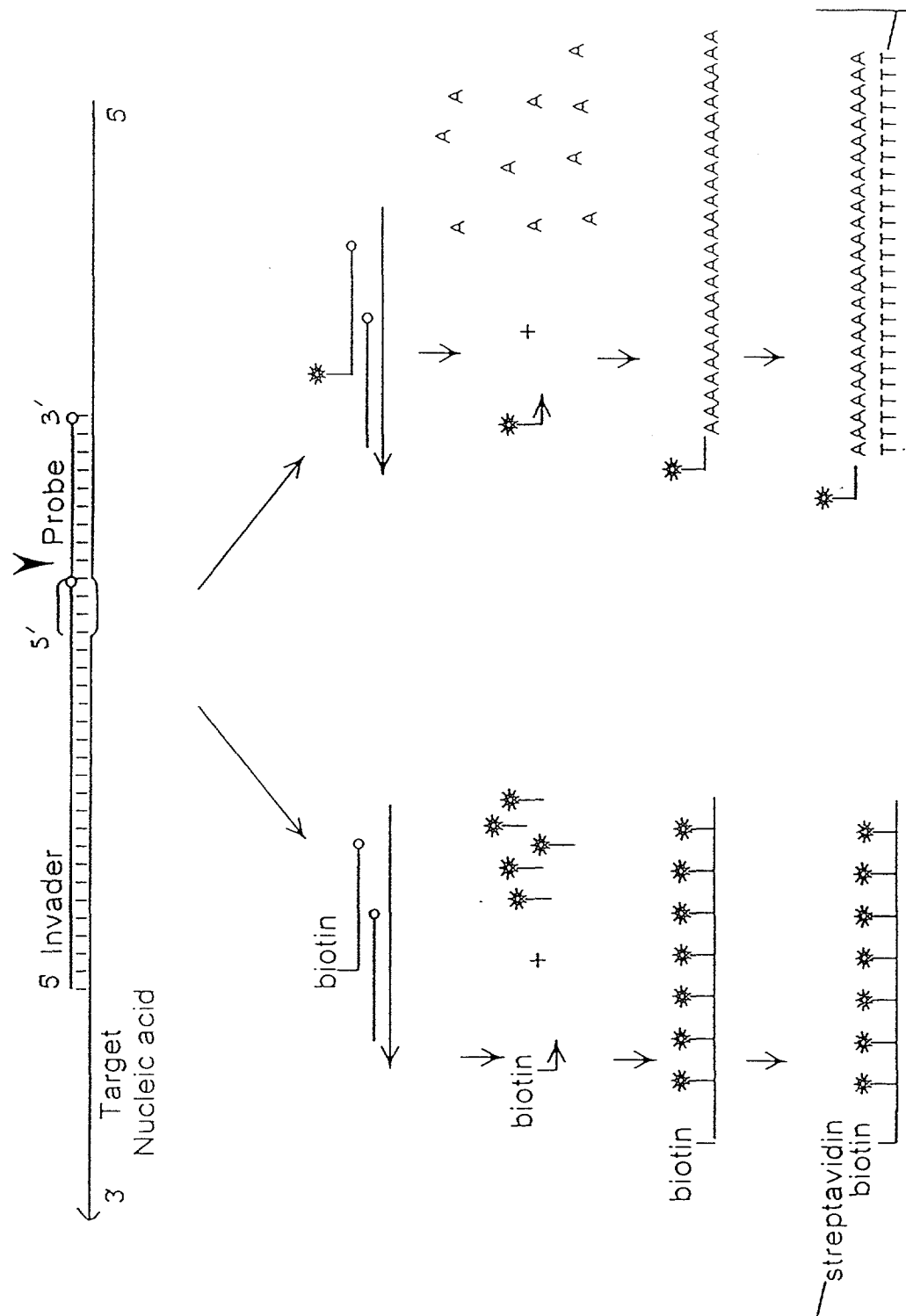


FED

78/127

009007 5348960

FIGURE 67



009007 50E48960

FIGURE 68

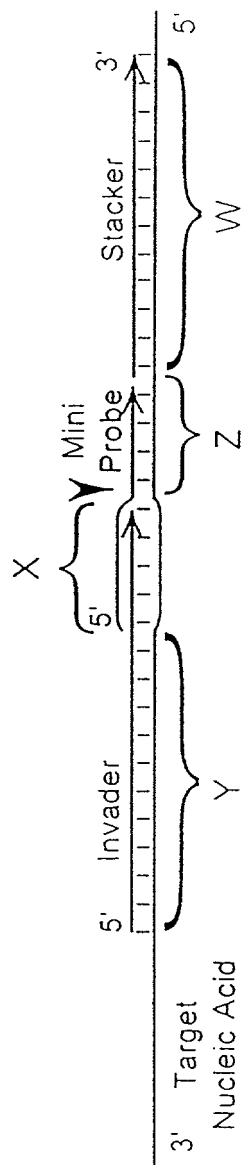
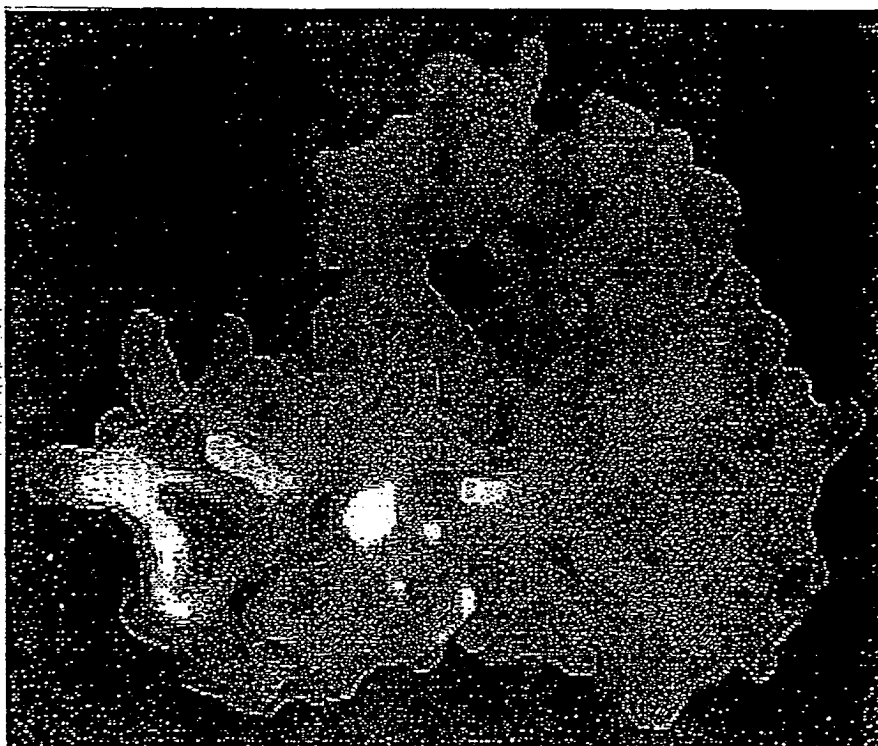




FIGURE 69



09684305-100600

81/127

009007" 5043960

FIGURE 70-A

	10	20	30	40	50	60	70																
MGVO	----	FGDF	IPK	--NI	SFED	LKGG	KKVA	IDGM	NAL	YOFL	TSIR	LDGS	PLNR	KCEI	TSAY	NGV	FY	MJAF	ENI	PRO			
MGVP	----	IGEI	IPR	--KE	IENL	YGKK	IAID	ALNA	YOFL	STIRO	KDGT	PLMD	SKGR	ITSH	L	SGL	FY	PFUF	ENI	PRO			
MGIO	GLAK	LIAD	VAPSA	I	REND	IKSY	FGRK	VAID	ASMS	YOFL	IAVRO	-GGD	V	LN	EEGE	TTSH	LMGM	FY	HUMF	ENI	PRO		
MGIH	GLAK	LIAD	VAPSA	I	REND	IKSY	FGRK	VAID	ASMS	YOFL	IAVRO	-GGD	V	LN	EEGE	TTSH	LMGM	FY	MUSF	ENI	PRO		
MGIK	GLNA	I	SEHV	PSA	I	RKSD	IKSF	FGRK	VAID	ASMS	YOFL	IAVRO	OD	GGOL	TNEA	GETT	SHLM	GMFY	YST5	10	PRO		
MGVH	SFWD	DIAG	----	PTAR	PVR	LES	LED	KRM	AVD	AS	WIYOF	LKAV	RO	DOEG	NAV	KN	----	SHIT	GF	FR	YSTR	AD2	PRO
MGVS	GLWN	ILE	----	PVKR	PKLE	TL	VNKR	LAID	AS	WIYOF	LKAV	RD	KEGN	OLKS	----	SHV	VG	FFR	SPOR	AD13	PRO		
MGVO	GLWK	LLE	----	CSGR	VS	PEAL	EGK	ILAV	DIS	WLNO	AL	KGVR	DRH	GS	NIEN	----	PHLL	TL	LFH	HUMX	PG	PRO	
MGVO	GLWK	LLE	----	CSGR	VS	PEAL	EGK	VLAV	DIS	WLNO	AL	KGVR	DRH	GS	NIEN	----	AHLL	TL	LFH	MUSX	PG	PRO	
MGVO	GLWK	LLE	----	CSGR	PI	NP	GT	LECK	ILAV	DIS	WLNO	AV	KGAR	DR	OG	NAION	----	AHLL	TL	LFH	XENX	PG	PRO
MTIN	GIWE	WANH	VV	----	RKVP	NET	MRD	KTLS	IDGH	IWL	YESL	KGCE	AH	HOOT	----	PNSY	LV	VTFT	CEL	RAD2	PRO		

	80	90	100	110	120	130	140																				
4	KT	IHL	LEND	I	TP	IW	VDGE	PPKL	KEK	TRK	VRR	EMKE	AE	LK	ME	AIKK	----	EDF	EEA	KYAK	RVS	YLTP	MJAF	ENI	PRO		
4	RT	INL	MEAG	IKP	VY	VDGE	PPFK	KKKE	LEK	RR	EA	REEA	EE	KE	WRE	ALEK	----	GEI	EE	ARK	YAOR	ATRV	NE	PFUF	ENI	PRO	
0	RT	IRM	ENG	IKP	VY	VDG	KPP	OLK	SGEL	AKR	SERR	AE	AE	KOL	OOA	AA	----	GAE	OE	VEK	FTKRL	VKVT	K	HUMF	ENI	PRO	
9	RT	IRM	-ENG	IKP	VY	VDG	KPP	OLK	SGEL	AKR	SERR	AE	AE	KOL	OOA	OE	----	GME	EE	VEK	FTKRL	VKVT	K	MUSF	ENI	PRO	
1	RTL	MID	NG	IKP	CV	VDG	KPP	OLK	SHEL	TKR	SSRR	VET	TEK	KL	----	EA	----	TTE	LEK	MK	OE	RRL	VKVS	K	YST5	10	PRO
1	RICK	LLY	FG	IR	PI	V	FDG	GV	PLK	RET	I	ORKER	ROG	KRES	AKST	ARK	LLAL	OLONG	SND	NK	RDS	DEV	TM	YSTR	AD2	PRO	
1	RICK	LLFF	GI	KP	V	FDG	GAP	SLK	ROT	I	OKR	ARR	LD	REEN	ATV	TANK	LLAL	OMR	HOA	MLL	KRD	AD	EV	TO	SPOR	AD13	PRO
1	RLCK	LLFF	RI	PI	F	VDG	DAP	LLK	KOT	L	VKR	ROR	KOL	ASS	DSR	KTTE	KLK	TFL	KROA	IKTER	IAAT	VTG		HUMX	PG	PRO	
1	RLCK	LLFF	RI	PI	F	VDG	DAP	LLK	KOT	L	VKR	ROR	KOL	ASS	DSR	KTTE	KLK	TFL	KROA	IKTER	IAAT	VTG		MUSX	PG	PRO	
1	RLCK	LLFF	RI	PI	F	VDG	DAP	LLK	KOT	L	VKR	ROR	KOL	ASS	DSR	KTTE	KLK	TFL	KROA	IKTER	IAAT	VTG		XENX	PG	PRO	
0	R	IOR	LLE	LK	I	P	I	V	FDN	I	NASS	SAH	ESK	DONE	FV	PRK	RRS	FGD	SP	TNL	V	----	----	----	CEL	RAD2	PRO

FIGURE 70-B

	150	160	170	180	190	200	210	
130	KMVENCKYLLSLMGIPYVEAPSEGEAOASYMAKKGQVWVVSODYDALLYGAPRVVRNLTTTKEM----							MJAFENI . PRO
130	MLIEDAKKLLLELMGIPIVOAPSEGEAOAAAYMAAKGSVYASASODYDSLLFGAPRLVRNLTTGKRKLPGK							PFUFENI . PRO
136	OHNDECKHLLSLMGIPYLDAPSEAEASCAALVKAGKVYAAATEOMDCLTFGSPVLMRHLTASEAKKLPIO							HUMFENI . PRO
134	OHNDECKHLLSLMGIPYLDAPSEAEASCAALAKAGKVYAAATEOMDCLTFGSPVLMRHLTASEAKKLPIO							MUSFENI . PRO
134	EHNEEAOKLLGLMGIPYIAPTEAEAOCAELAKKGKVYAAASEMDTLCYRTPFLLRHLTFSEAKKEPIH							YST510 . PRO
131	DMIKEVOELLSRFGIPYITAPMEAEAOCAELLOLNLVDGII TDOSDVLFGGTKIYKNMFHEKNY----							YSTRAD2 . PRO
131	VMIKECOELLRLFGIPYIVAPOEAEAOCSKLELKLVDGIVTDOSDVLFGGTRVYRNMFNONKF----							SPORAD13 . PRO
131	OMFLESOEELLRLFGIPYIOAPMEAEAOCAILDLTDOOTSGTITDOOSDIWLFGARHVYRNFNKNKF----							HUMXPG . PRO
131	OMFLESOEELLRLFGIPYIOAPMEAEAOCAVLDLSOOTSGTITDOOSDIWLFGARHVYKNNFNKNKF----							MUSXPG . PRO
131	OMCLESOELLRLFGIPYIVAPMEAEAOCAILDLTDOOTSGTITDOOSDIWLFGARHVYKNNFFSONKH----							XENXPG . PRO
111	DHVKYKNALLTELGIKVIAPGDGEAOCARLEDLGVTSGCITTDIFYFLFGGKNLYRFDFTAGT-----							CELRAD2 . PRO
195	-----PELIELNEVLEDLRISLDDLIDIAIFMGTDYNPGGV--K--GIGFKRAYELVRSGVAK--DV							MJAFENI . PRO
200	NYVE- IKPELILEEVLEKELKTREKLIELAILVGTDYNPGGI--K--GIGLKKALEIVRHSKODPLAKF							PFUFENI . PRO
206	EFHLSRILOEGLNOEOFVDLCLLGSDYCESIRGIGPKRAVDL IOK--HKSIEEIVRRLOPN-----KY							HUMFENI . PRO
204	EFHLSRVLOELGLNOEOFVDLCLLGSDYCESIRGIGAKRAVDL IOK--HKSIEEIVRRLOPN-----KY							MUSFENI . PRO
204	EIDTELVRGLDLTIEOFVDLCLMLGSDYCESIRGVGPVTALKIKT--HGSIEKIVEFIESGESNNTKW							YST510 . PRO
198	FYDAESILKLLGLDRKNMIELAOLLGSDYTNGLKMGMPVSSIEVIAEF--GNLKNFKDWYNNGOFODKRK							YSTRAD2 . PRO
198	LYLMDDMKREFNVNOMDLIKLAHLGSDYTMGLSRVGPVLALEILHEFPDGTGLFEFKKWFORLSTGHAS							SPORAD13 . PRO
198	YYQYVDFHNOGLDRNKLINLAYILGSDYTEGIPTVGCVTAMEILNEFPGHGLEPLLKFESEWHEAOKNP							HUMXPG . PRO
198	YYQYVDFYSOLGLDRNKLINLAYILGSDYTEGIPTVGCVTAMEILNEFPGRGLDPLLKFESEWHEAONNK							MUSXPG . PRO
198	YYQYADIHNOGLDRSKLINLAYILGSDYTEGIPTVGVVSAMEILNEFPGOGLEPLVKFEKWSEAOOKK							XENXPG . PRO
175	-----SSTACLHDIHLSLGRMF-----							CELRAD2 . PRO

FIGURE 70-C

251	LKKEVEYYDEIKRIFKEPKV	290	300	310	320	330	340	350	MJAFEN1 PRO
265	OKOSVDLYAIKEFFLNPPV	290	300	310	320	330	340	350	PFUFEN1 PRO
269	PVPENWLHKEAHOLFLEPEV	290	300	310	320	330	340	350	HUMFEN1 PRO
267	PVPENWLHKEAOLFLPEV	290	300	310	320	330	340	350	MUSFEN1 PRO
272	KIPEDWPYKOARMFLDPEV	290	300	310	320	330	340	350	YST510 PRO
265	OETENKFEKDLRKKLVNNEI	290	300	310	320	330	340	350	YSTRAD2 PRO
268	KNDVNTPVKKRINKLVGK-I	290	300	310	320	330	340	350	SPORAD13 PRO
268	KIRPNPHDTKVKKKL--RTLO	290	300	310	320	330	340	350	HUMXPG PRO
268	KVAENPYDTKVKKKL--RKL	290	300	310	320	330	340	350	MUSXPG PRO
268	KMRPNPNDTKVKKKL--RLD	290	300	310	320	330	340	350	XENXPG PRO
194	-----EKKVSRPHLISTAIL	290	300	310	320	330	340	350	CELRAD2 PRO

84/127

300	RVKKHVDKLYNLIA--	360	370	380	390	400	410	420	MJAFEN1 PRO
314	RVKNGLERLKKAI--	360	370	380	390	400	410	420	PFUFEN1 PRO
320	RIRSGVKRLSKSROGS-TO	360	370	380	390	400	410	420	HUMFEN1 PRO
318	RIRSGVKRLSKSROGS-TO	360	370	380	390	400	410	420	MUSFEN1 PRO
323	RVKSGISRLKKGKLSG-IO	360	370	380	390	400	410	420	YST510 PRO
335	KSDEILPLIRDVNKRKK--	360	370	380	390	400	410	420	YSTRAD2 PRO
337	RTNEVLLPVIODMHKKOF--	360	370	380	390	400	410	420	SPORAD13 PRO
336	KTDESFPVLKOLDAOOTOL	360	370	380	390	400	410	420	HUMXPG PRO
336	KTDESLYPVLKHLNAHOTOL	360	370	380	390	400	410	420	MUSXPG PRO
336	KTDEVLLPVLKOLNAOOTOL	360	370	380	390	400	410	420	XENXPG PRO
257	EIPARSEDORKLRLRRKKYN	360	370	380	390	400	410	420	CELRAD2 PRO

General Information		Demographics		Clinical History		Physical Examination		Laboratory Studies		Imaging Studies		Treatment		Outcome		
Item	Value	Item	Value	Item	Value	Item	Value	Item	Value	Item	Value	Item	Value	Item	Value	
Age	45	Sex	Male	Chief Complaint	Headache	Location	Right side	Duration	3 days	Severity	7/10	Associated Symptoms	Nausea	Yes	Frequency	3 times
Weight	180	Height	70	Medical History	Hypertension	Medications	Lisinopril	Physical Exam	Normal	Laboratory	Normal	Imaging	Normal	Treatment	Analgesics	Outcome
BMI	24.3	BP	140/90	Family History	Stroke	Allergies	None	Neurological	Normal	Pathology	Normal	Follow-up	Improved	Notes	Headache resolved	Discharge

FIGURE 70-D

	430	440	450	460	470	480	490
314	-	-	-	-	-	-	MJAFENI PRO
327	-	-	-	-	-	-	PFUFENI PRO
348	-	-	-	-	-	GSL	HUMFENI PRO
346	-	-	-	-	-	GSL	MUSFENI PRO
351	-	-	-	-	-	PK-T	YST510 PRO
357	KRINEFF	-	-	-	-	-	YSTRAD2 PRO
359	SNLTOFFEGGNTNVYAPRVAYHFKSKRLLENALSSFKNOISNOSPMSSEEIOADADAFGESKGSDELOSRIL	-	-	-	-	-	SPORAD13 PRO
006	EKEFELLDAKARKTOKRGITNTLEESSLKRRKRLSDSKRKNTCGGFLGETCLSESSDGSSEHAESSLM	-	-	-	-	-	HUMXPG PRO
006	EKEFELLODAKCKTOKRELPHYK-----KETSVPKRRRPSPSGNGGFLGDOPYCSESPOESSCEDGEGSSVM	-	-	-	-	-	MUSXPG PRO
003	ERECTNORKGOKTNTKS-----OGTKRRKPTECSOEDODPGGGFIGIELKTLSSKAYSSD-----	-	-	-	-	-	XENXPG PRO
022	MKECGWPATRTOKELALSIRRKVHLTTTVAOTRIPODFAATKSKNFPIVEPCESLEDYISANN-----I	-	-	-	-	-	CELRAO2 PRO

85/127

	500	510	520	530	540	550	560
14	-----	-----	-----	-----	-----	-----NKTKOKTL	MJAFENI PRO
27	-----	-----	-----	-----	-----	-----KSGKOSTL	PFUFENI PRO
52	SAKRKEPEPKGST	-----	-----	-----	-----	-----KKKAKTGAAG	HUMFENI PRO
50	SAKRKEPEPKGPA	-----	-----	-----	-----	-----KKKAKTGGAG	MUSFENI PRO
54	KEOLAAAKRAOE	-----	-----	-----	-----	-----NKKLNKNKNK	YST510 PRO
64	-----	-----	PREYISGDKKLN	TSKRISTATGKL	-----	-----KK	YSTRAD2 PRO
29	RRKMMASKNSSDSDSEDNFLASLTPKTNSSSI	SIENLPRKTKLSTLL	-----	-----	-----	-----KKP	SPORAD13 PRO
76	NVORRTAAKEPKTASDSONSVKEAPVKNGGATTSSSDSDDDGGKEKMVLVTARSVFGKKRRKLRARG	-----	-----	-----	-----	-----	HUMXPG PRO
69	SARORSAAESSKIGCSOVPOLVRDSPHGRGOCVSTSSSDSEGEDKAKTVLVTARPVFGKKRRKLRKSMK	-----	-----	-----	-----	-----	MUSXPG PRO
58	-----GSSSDAEDLP SGLIDKOSOSGIVGROKASNKVESSSSDDEDRTVMVTAKPVFOGKKTKSKTMKE	-----	-----	-----	-----	-----	XENXPG PRO
187	WMRKRKRSESP0ILOHHAKROVPDRK	-----	-----	-----	-----	-----RSVKIRAEKPYPTOVJ	CELRAO2 PRO

003007 50E48950

FIGURE 70-E

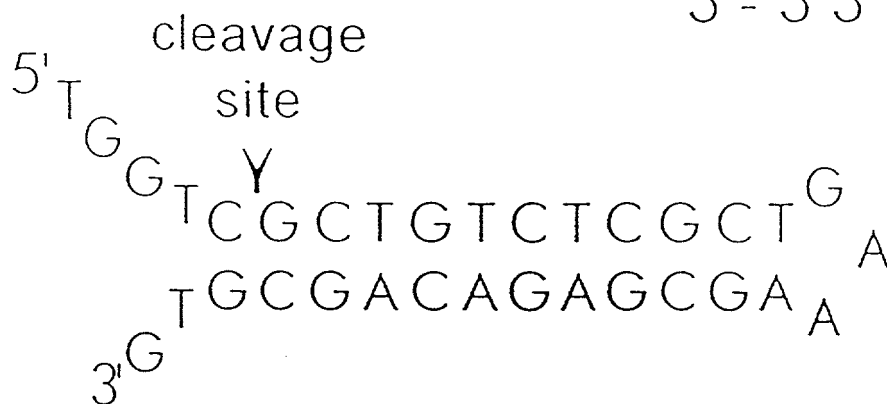
322 DAWFKZ
335 ESWFKR
375 KFKRGK
373 KFRRGK
377 VTKGRR
390 --RKM
483 SKRRRK
546 RKRTZ
538 RRKKKT
523 TVKRK
129 ELGOSD

86/127

MJAFENI PRO
PFUFENI PRO
HUMFENI PRO
MUSFENI PRO
YST510 PRO
YSTRAD2 PRO
SPORAD13 PRO
HUMXPG PRO
MUSXPG PRO
XENXPG PRO
CELRAD2 PRO

FIGURE 71

S - 3 3



1 1 - 8 - 0

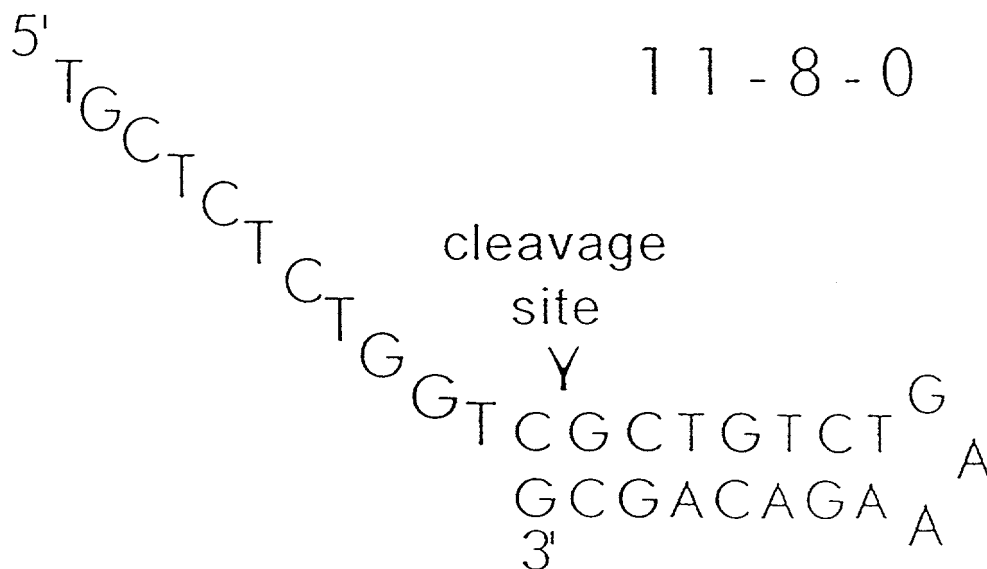
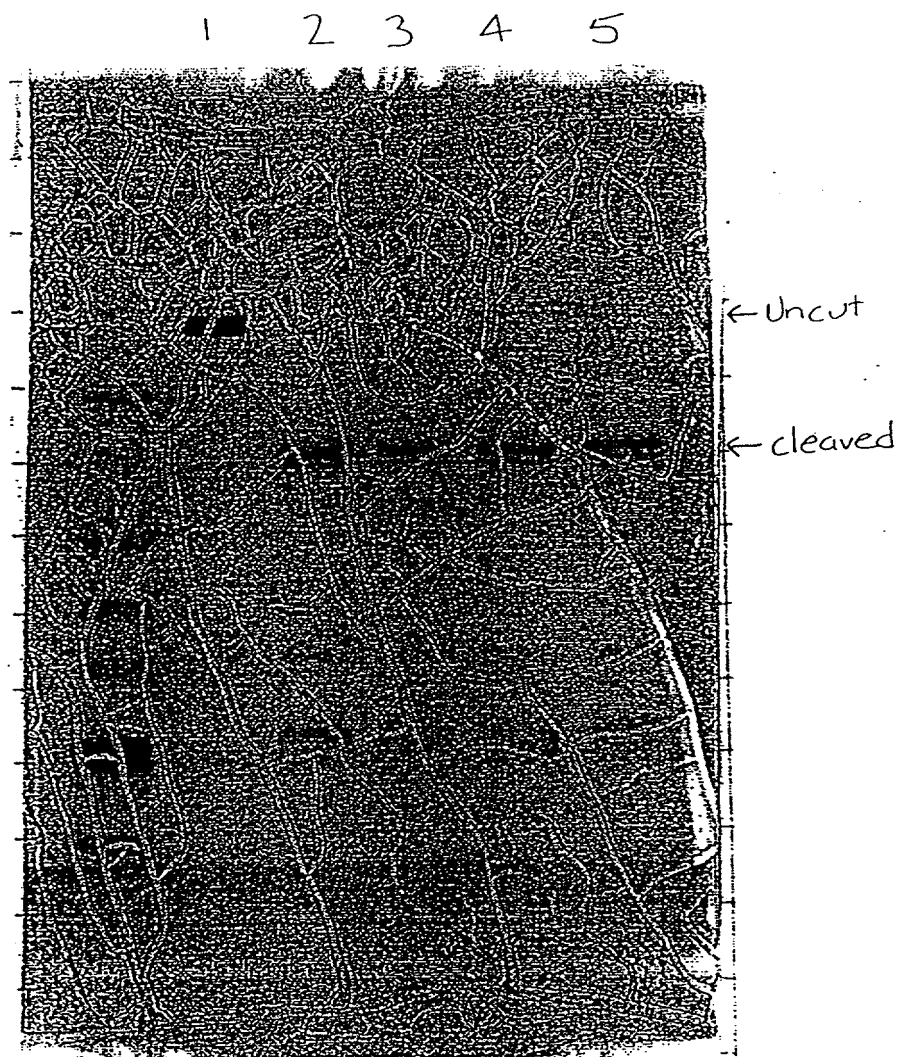
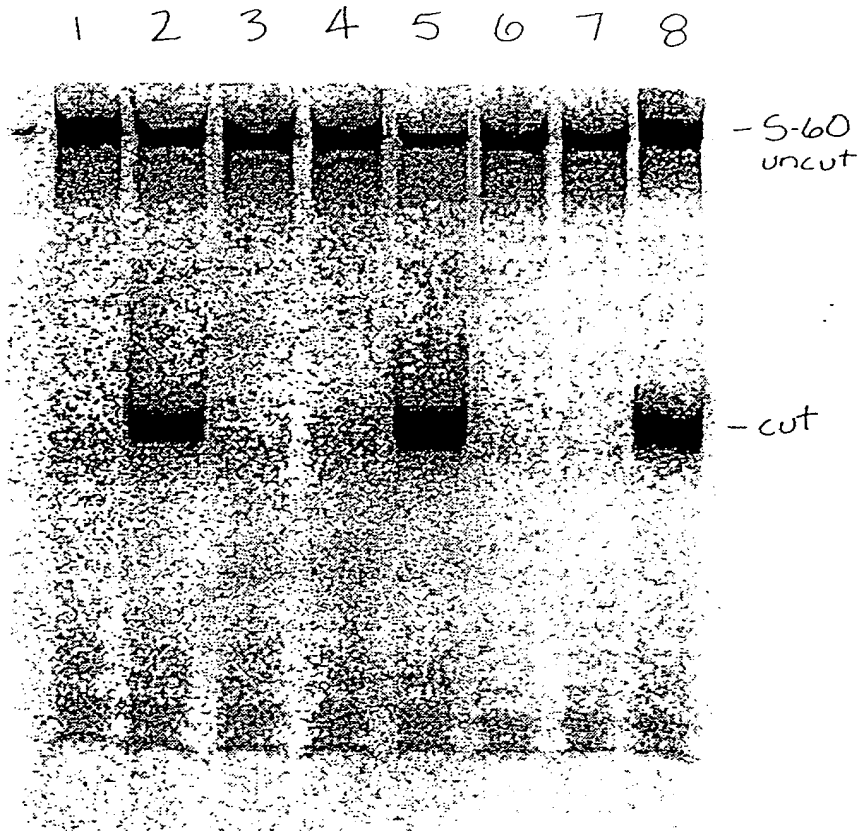


FIGURE 72



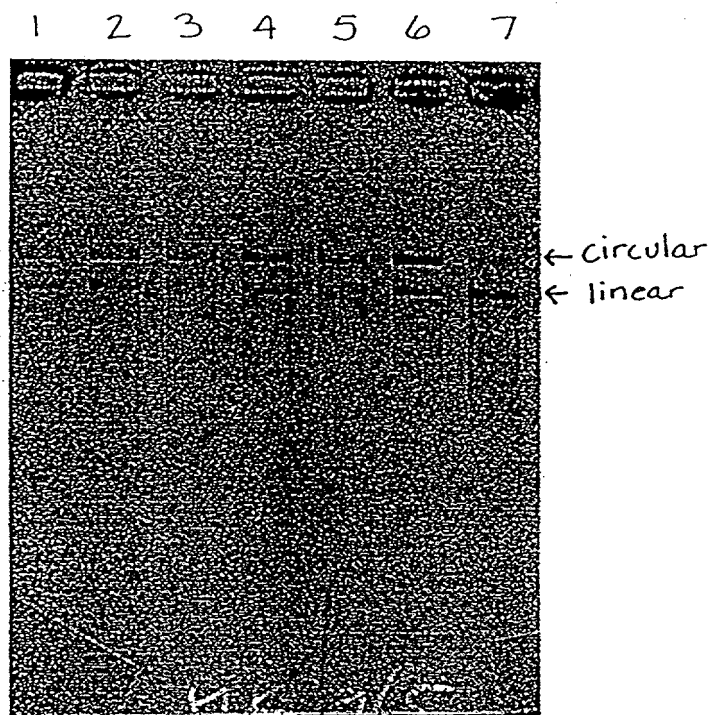
09664305-120600

FIGURE 73



00900T* 50E78960

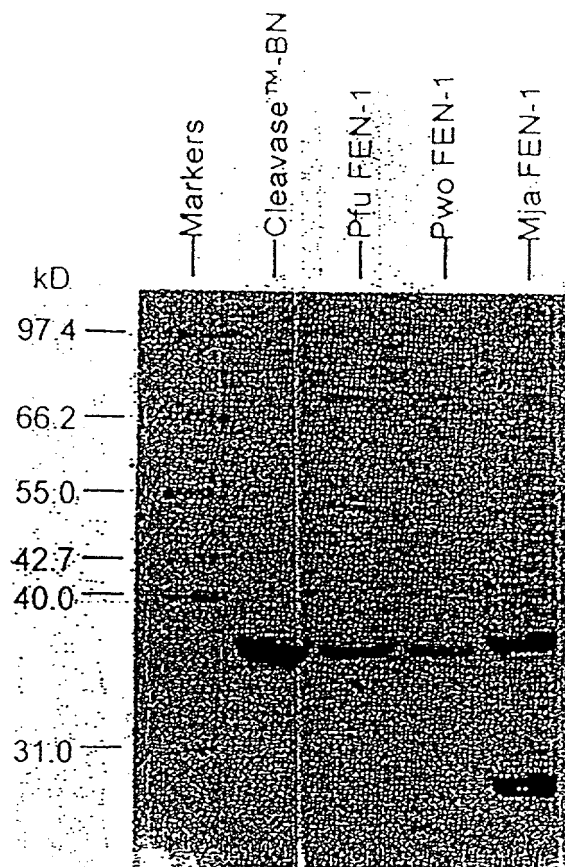
FIGURE 74



005007 50E48960

90/127

FIGURE 75

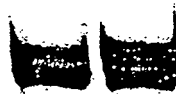


91/127

FIGURE 76

Enzyme

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BN



← 533 } uncut
← 11-8-0 }



← 11-8-0 } cut
← 533 }

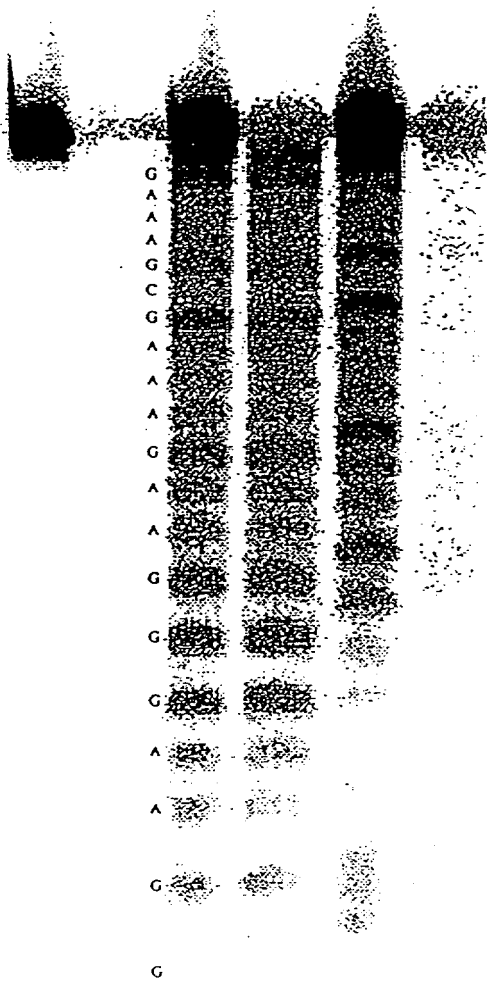
1 2 3

09684305-100600



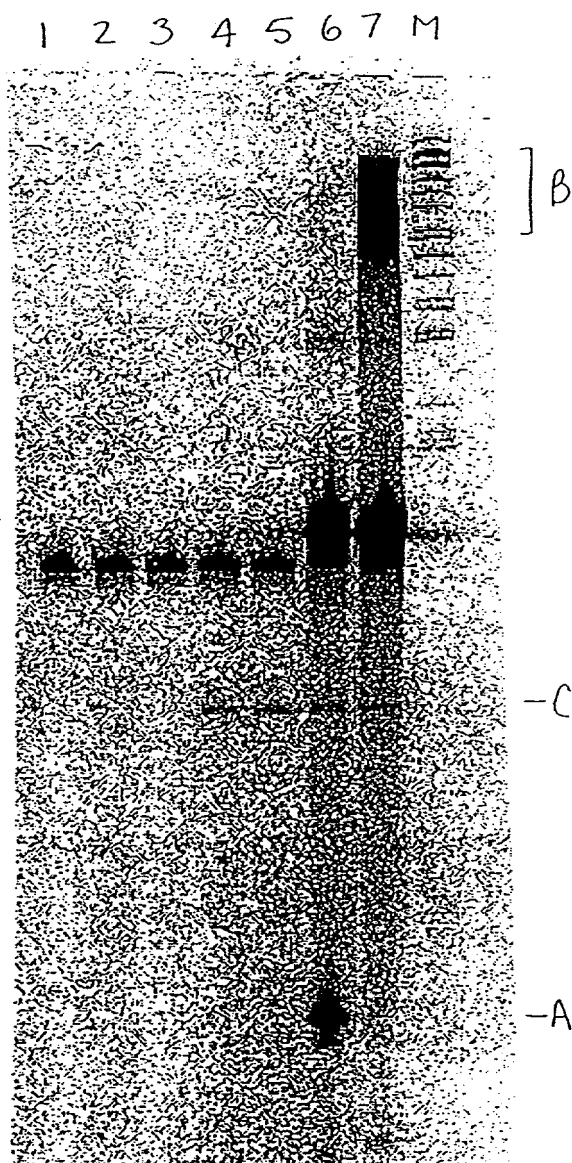
-	+	-	+	-	+
-	-	-	-	+	+
-	-	+	+	+	+

Terminal Transferase
Alkaline Phosphatase
Thermal Degradation



5'-nAGAAAggaaggga agaaagcgaaagG-3'

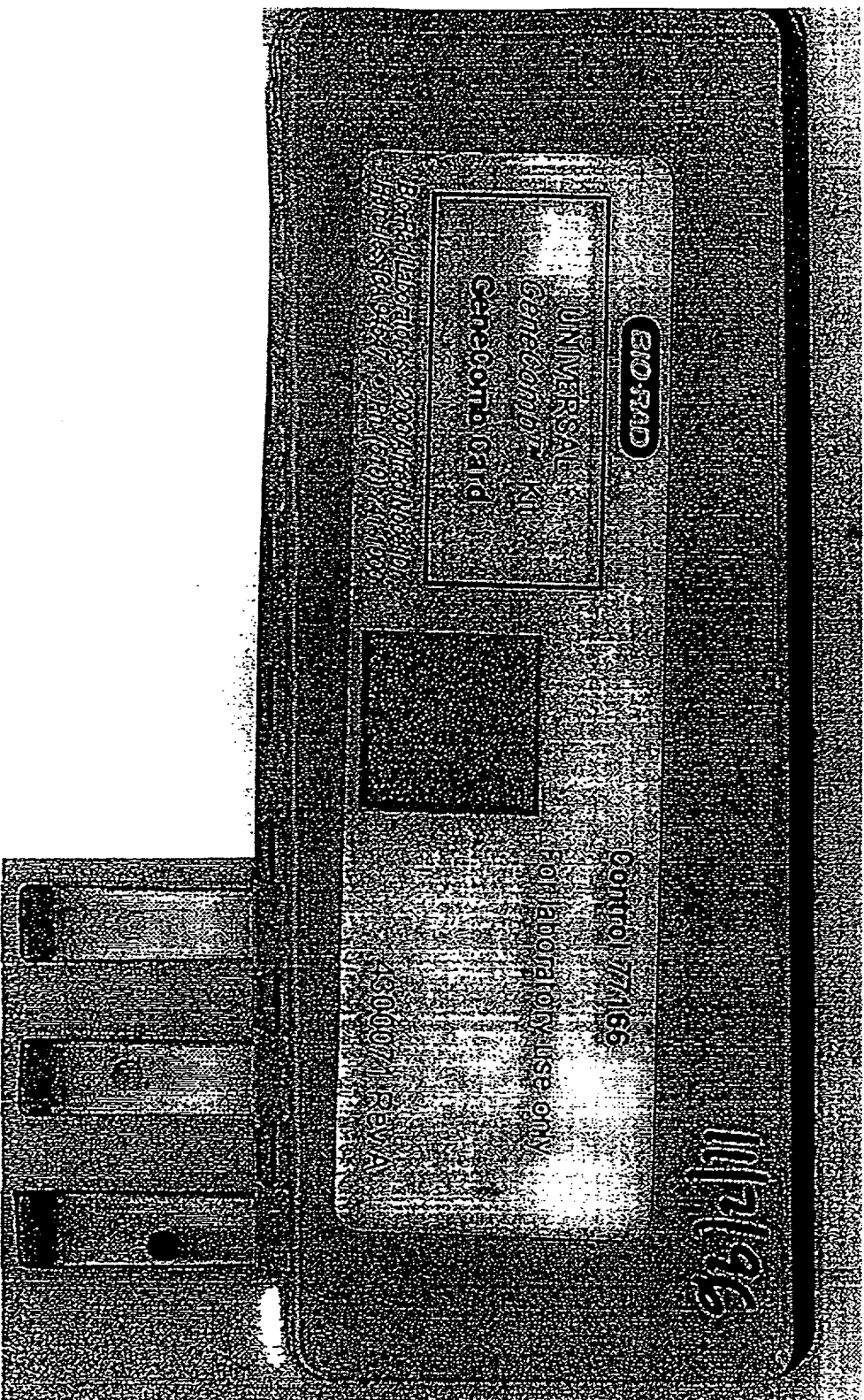
FIGURE 78



009001" 50E48960

94/127

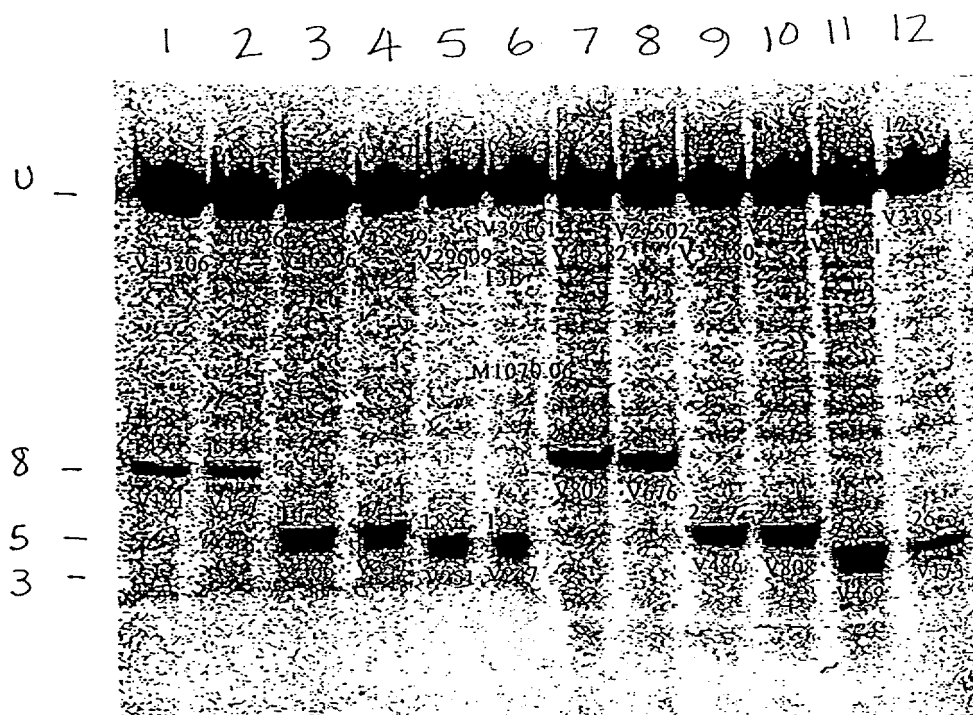
FIGURE 79



95/127

09684305 . 100600

FIGURE 80

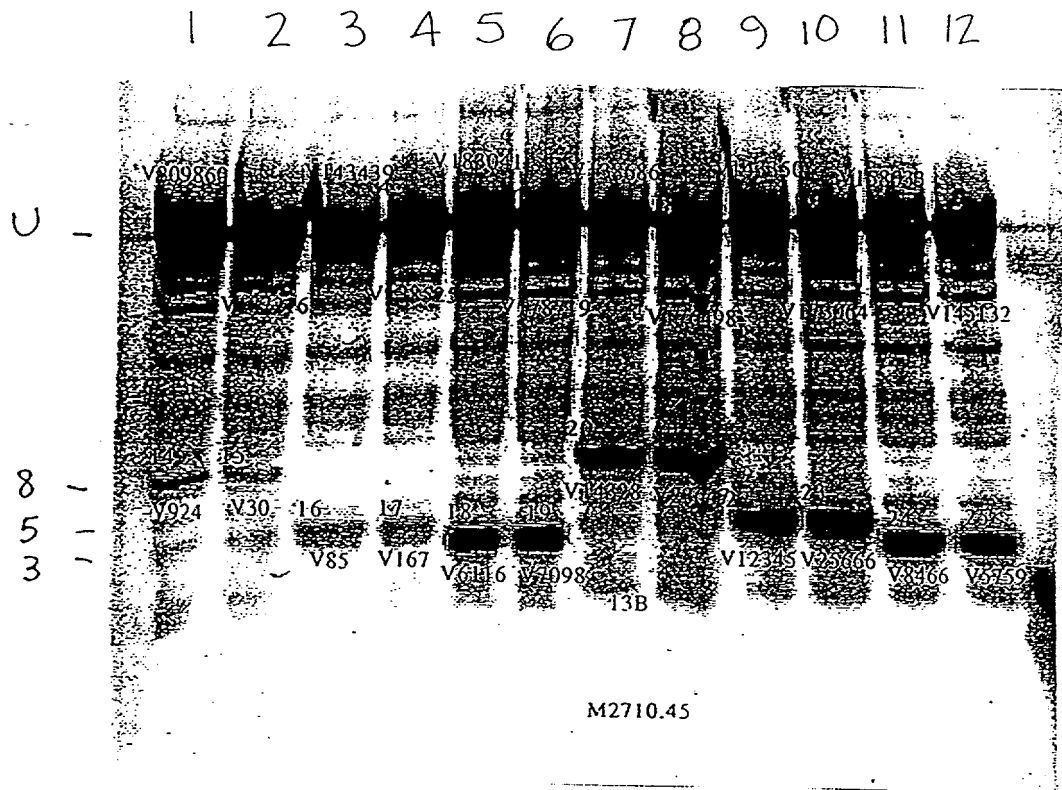


09684305.100600



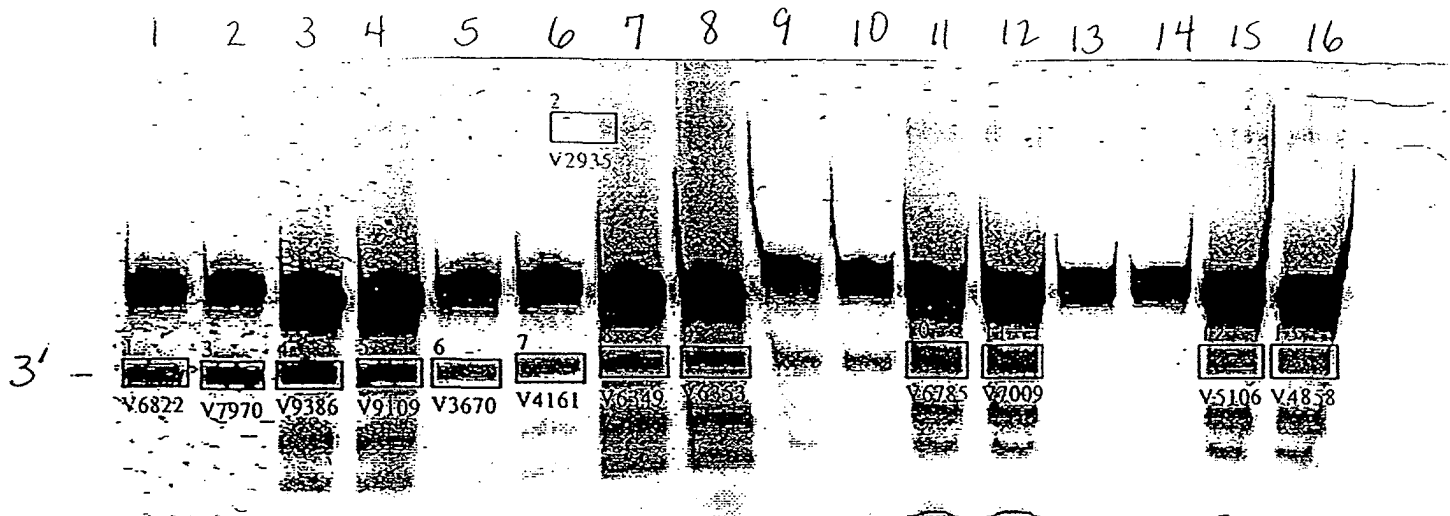
97/127

FIGURE 82



009001" 50579960

A



B

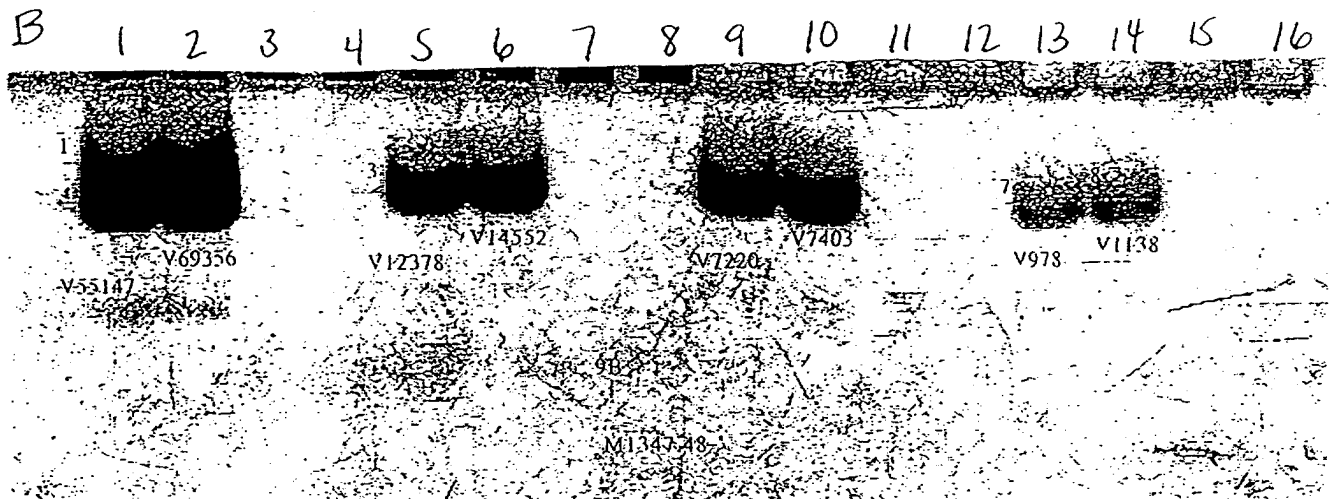
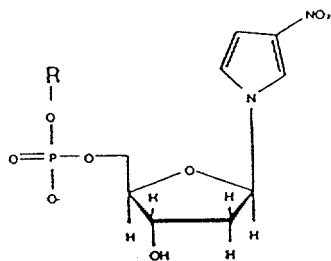
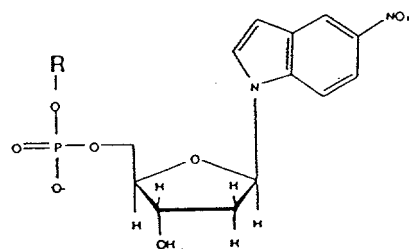


FIGURE 84



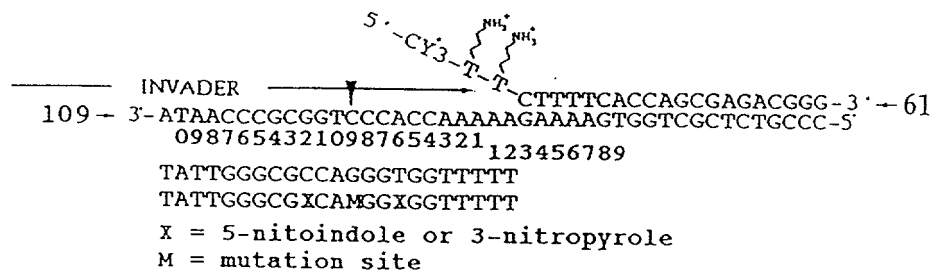
3-nitropyrrole



5-nitroindole




005430X-100500

FIGURE 85



0984305-109500

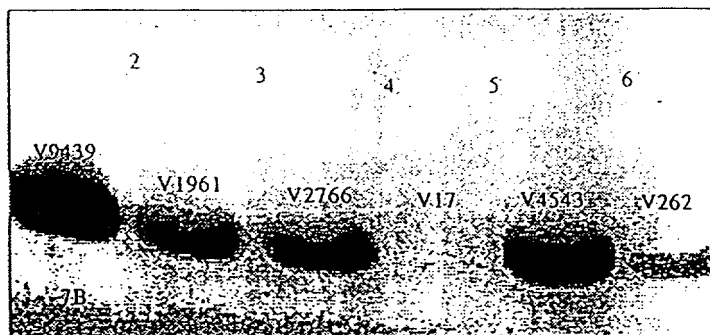
FIGURE 80

 1 Base Mismatch Allcomp 2 NI
 1 Base Mismatch Allcomp 1 NP
 1 Base Mismatch Allcomp 1 NP

Inval # 67 114 115 116 112 113

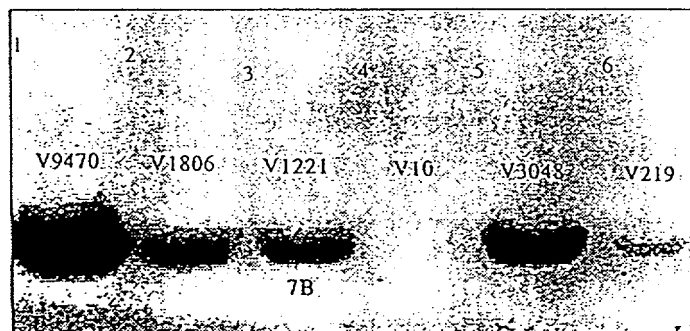
A

52°C



B

55°C



C

58°C

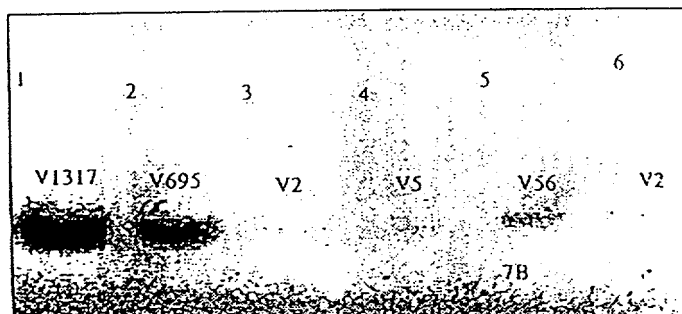




FIGURE 87

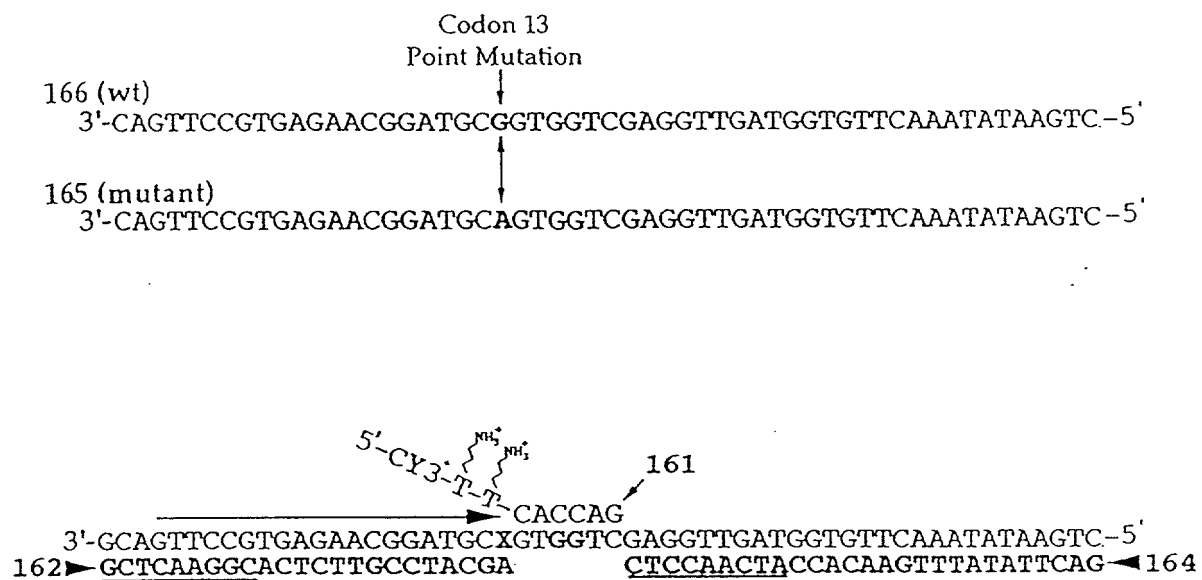


FIGURE 88

Temp	→	47°		50°		53°		56°		
Target	→	—	165	166	165	166	165	166	165	166

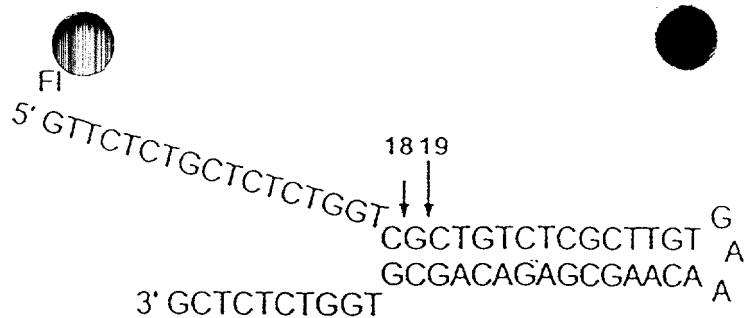


09684306 100600

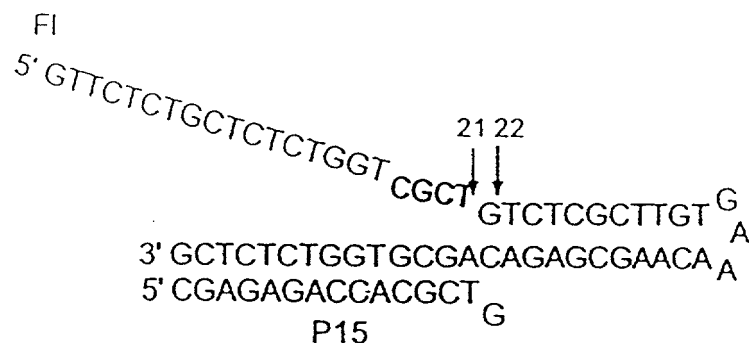
104/127

FIGURE 87

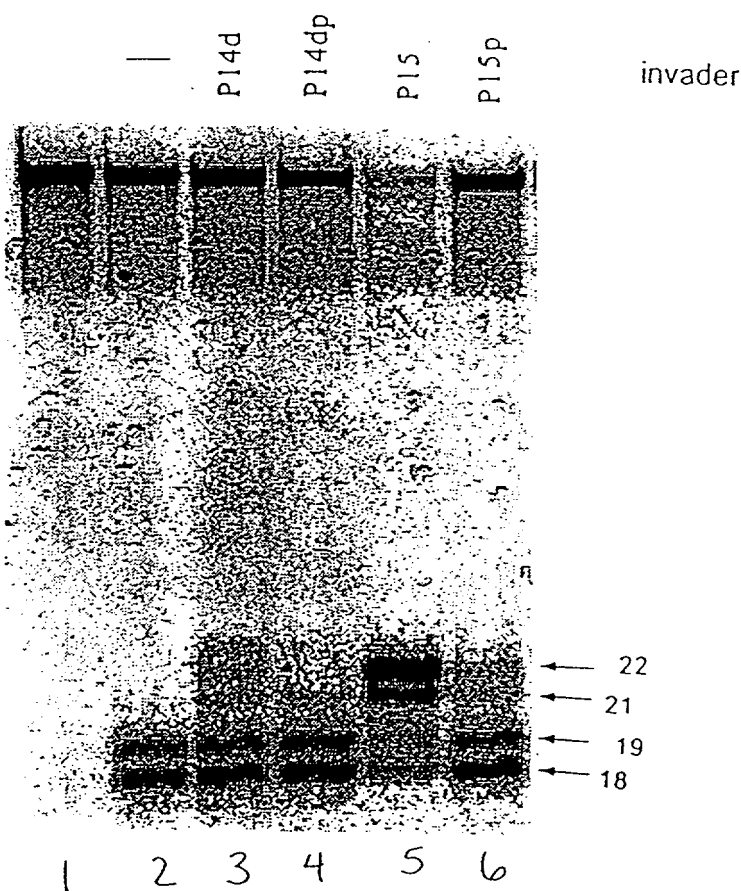
A



B



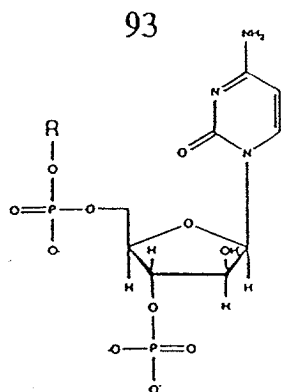
C



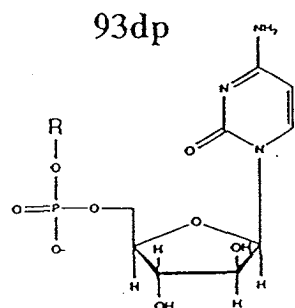
105/127

009007 50678950

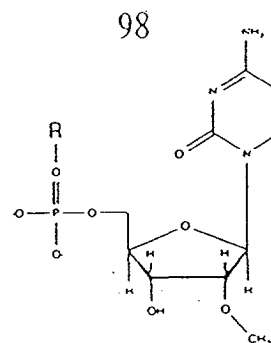
Invasader 3'-end Substituents



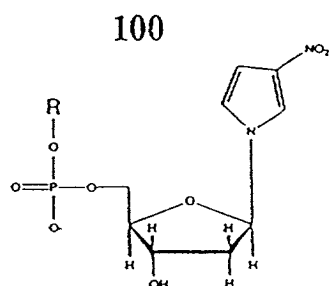
3'Phosphate C Arabinose



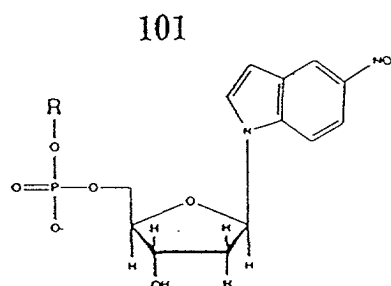
3'-Cytosine Arabinose



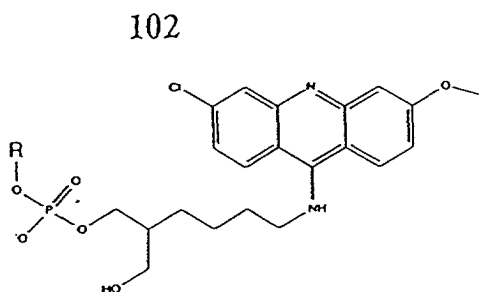
2'-Omethyl Cytosine



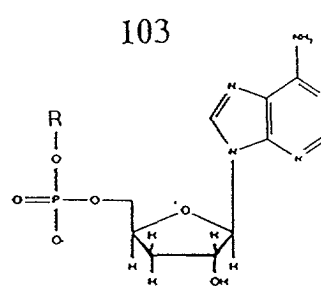
3-nitropyrrole



5-nitroindole

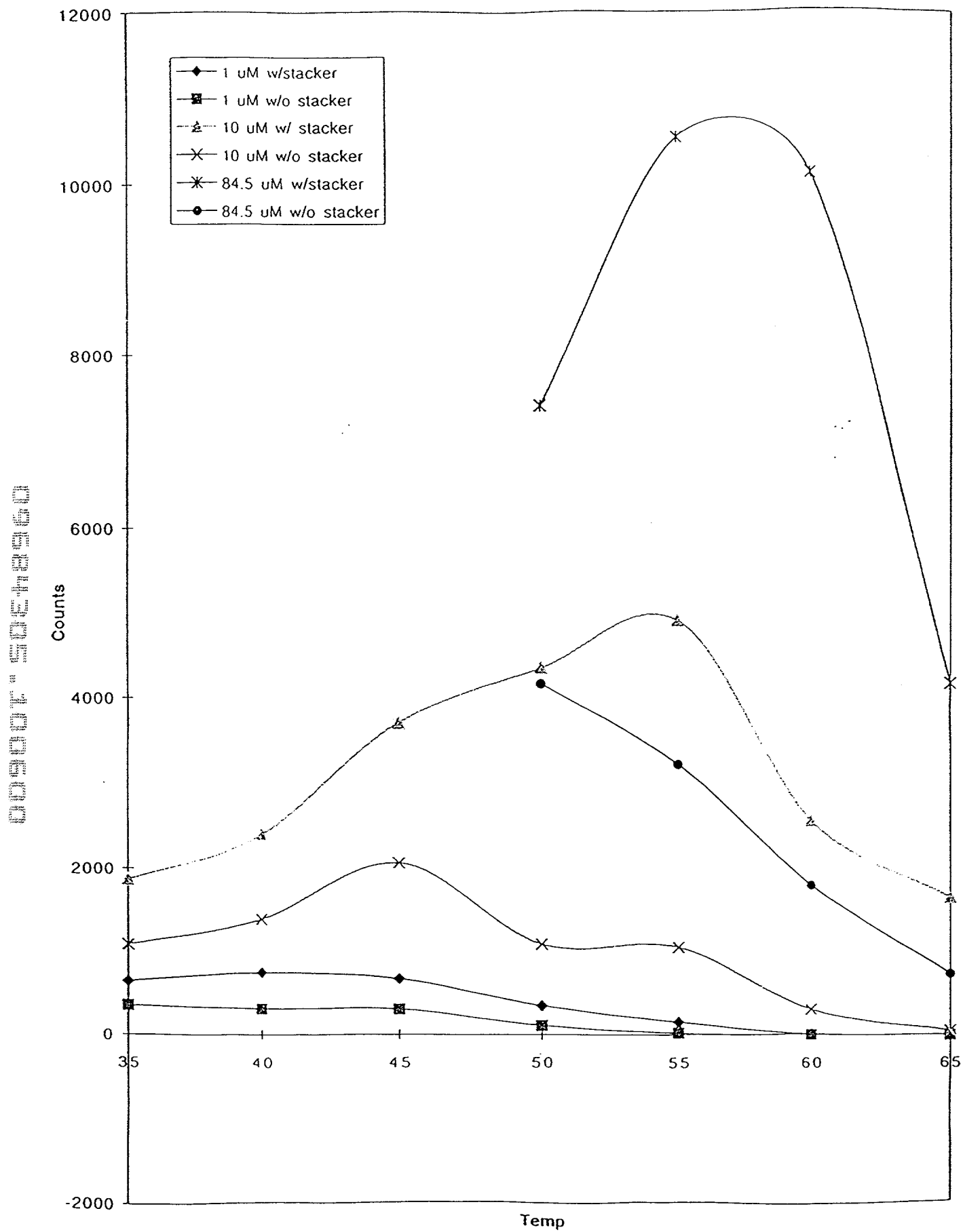


Acridine



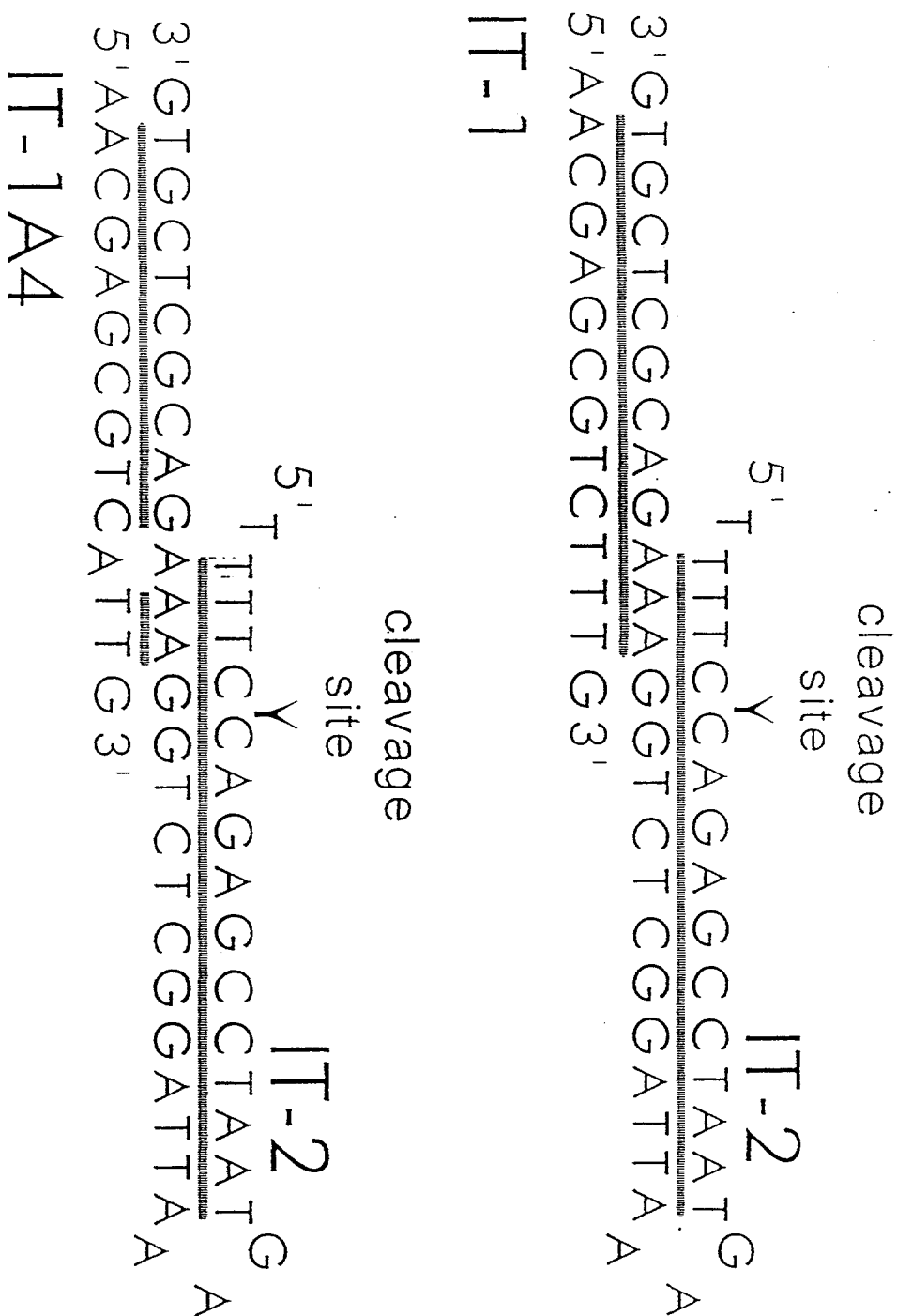
3'-deoxy-adenine

Concentration of Probe w/ and w/o Stacker Temp



107/127

FIGURE 92



108/127

FIGURE 93

1 2 3 4



-Uncut

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109/127

FIGURE 94

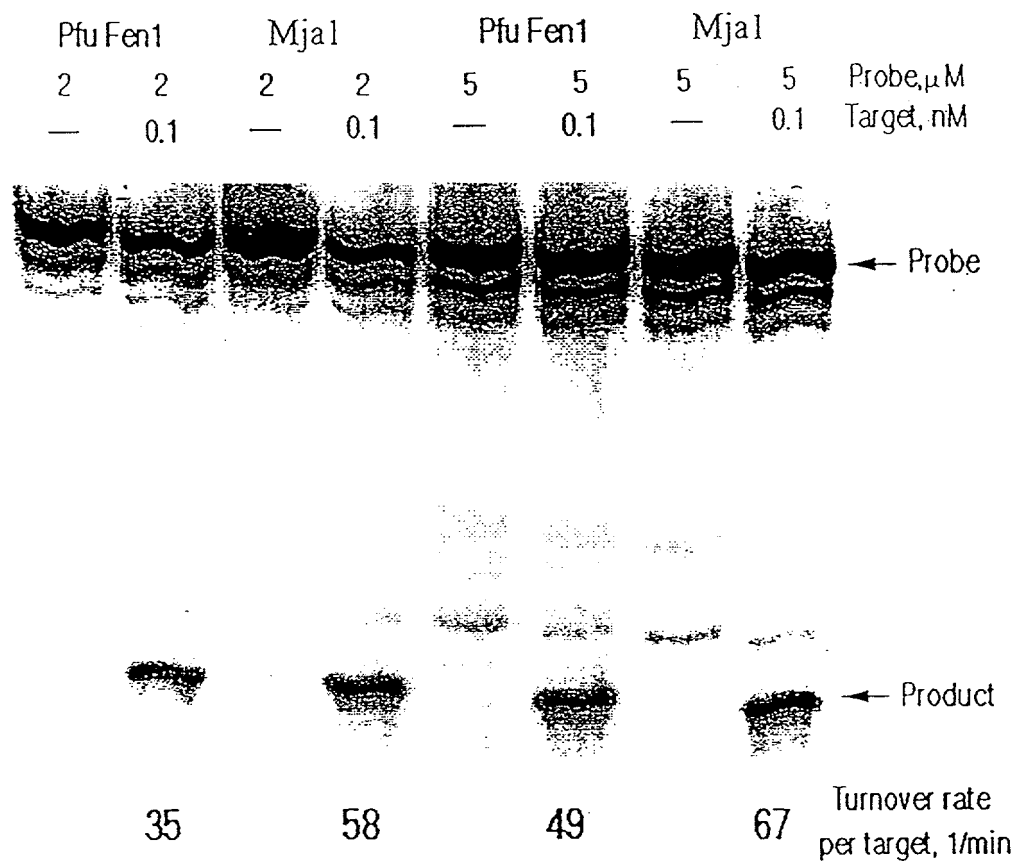
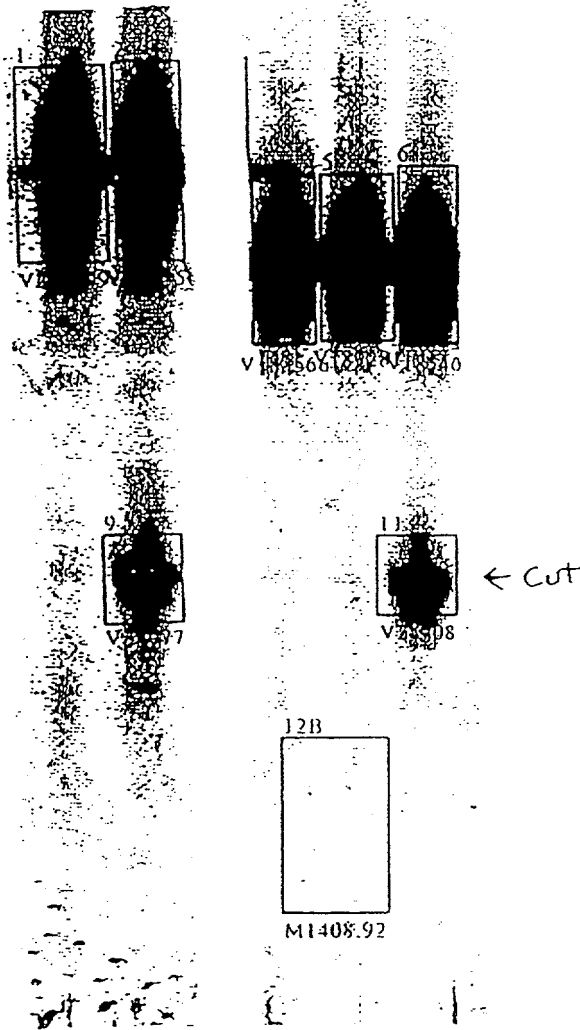


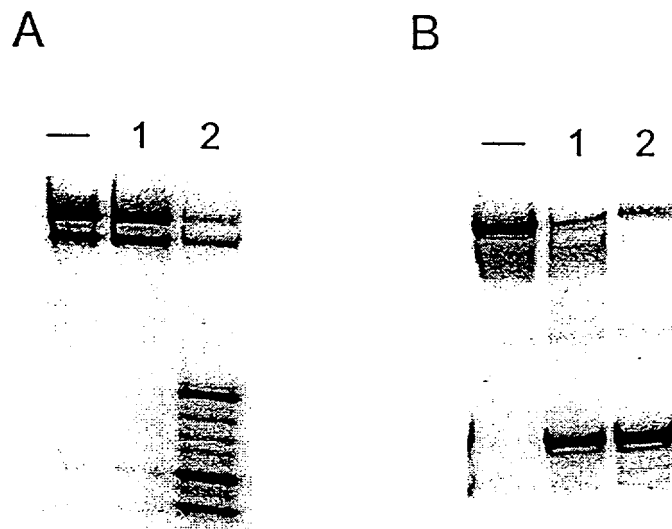
FIGURE 95

1 2 3 4 5



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FIGURE 96



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FIGURE 97

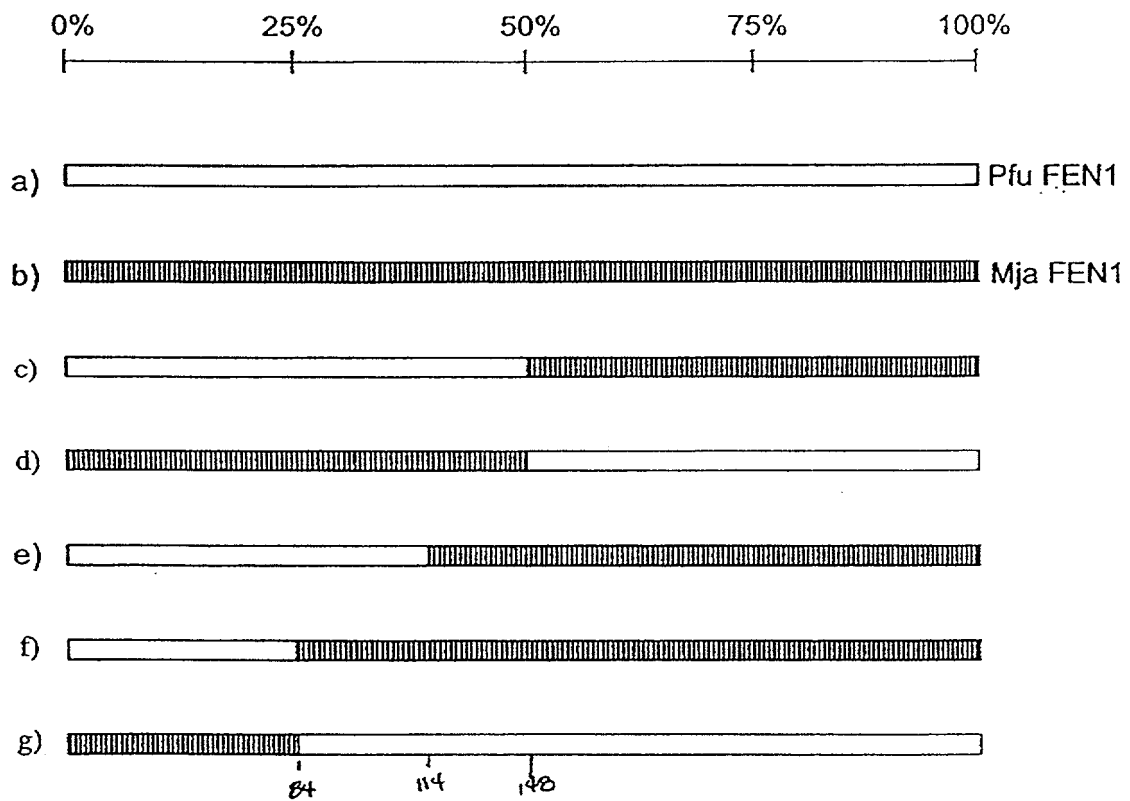


FIGURE 98A

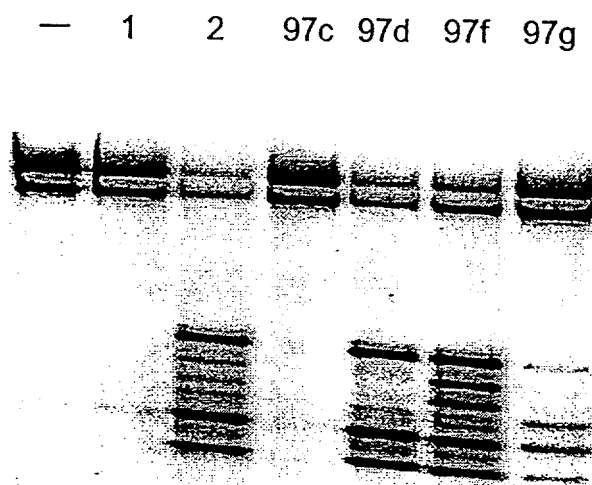
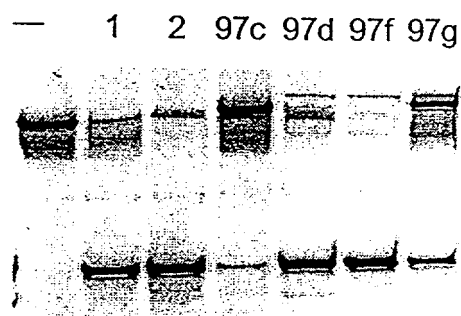


FIGURE 98B

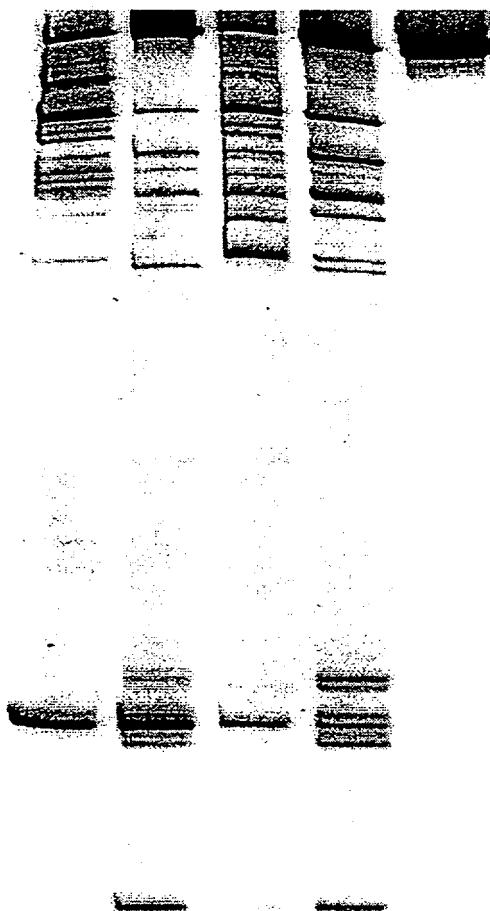


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FIGURE 99

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2 97d 97f —



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116/127

FIGURE 100

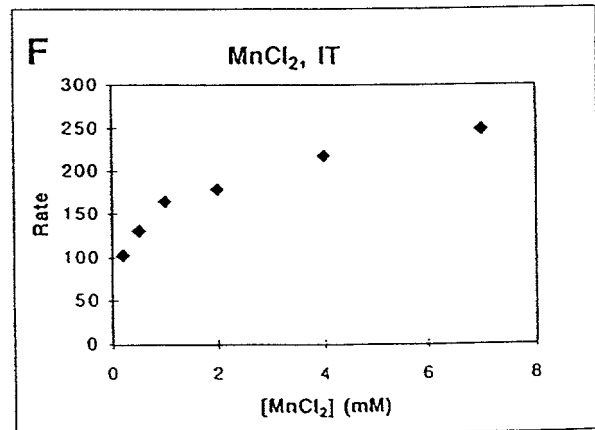
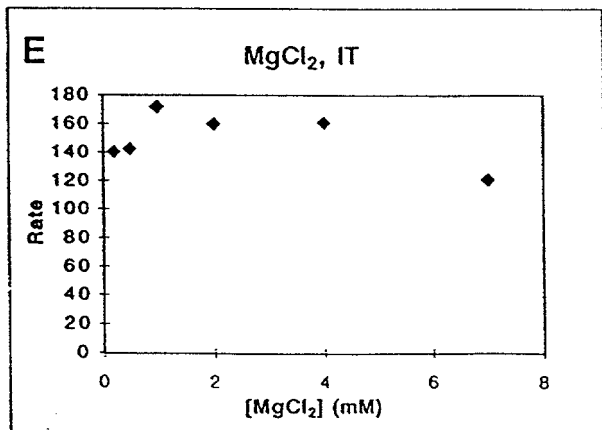
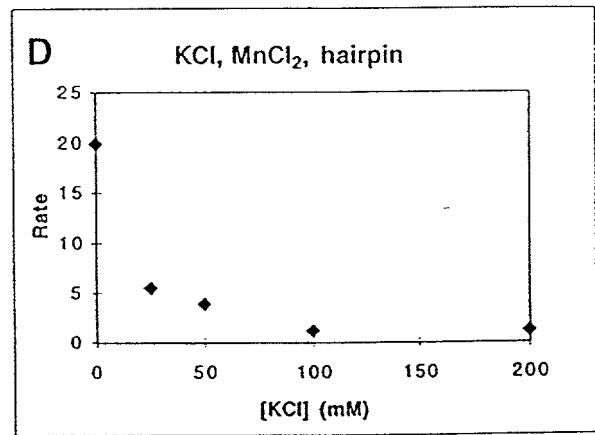
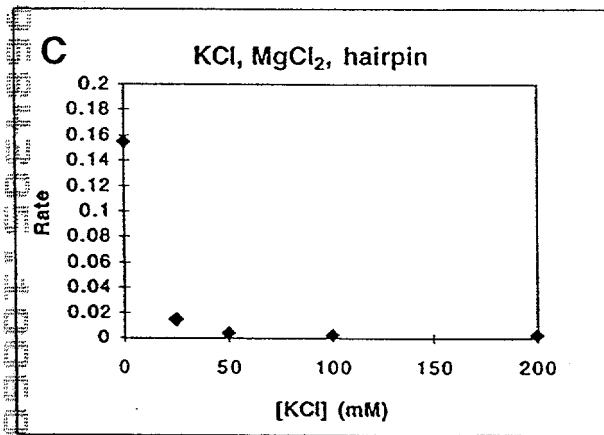
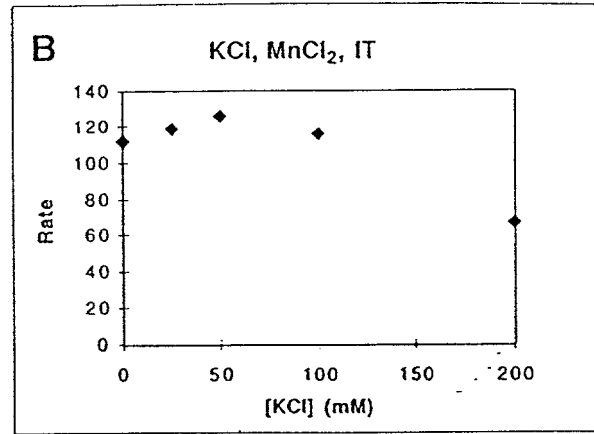
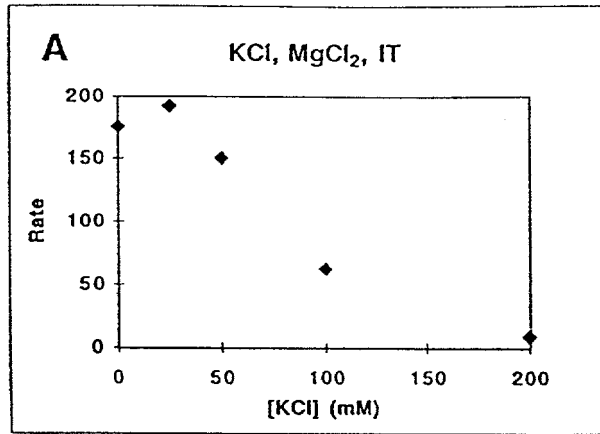


FIGURE 100 (cont.)

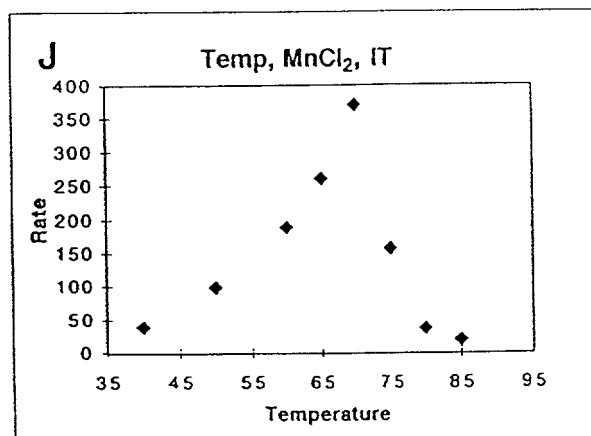
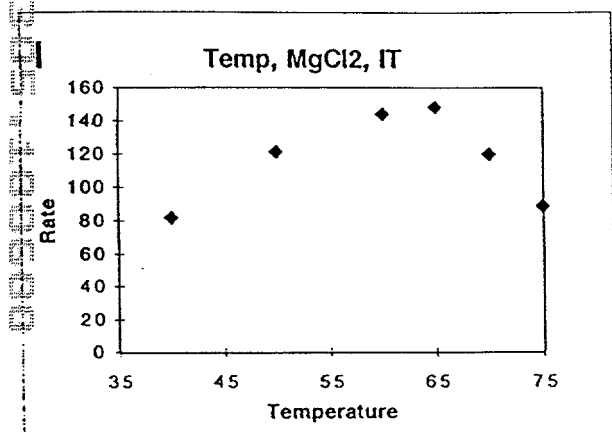
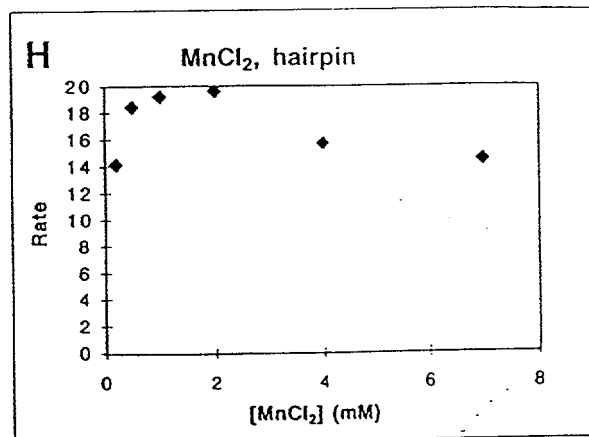
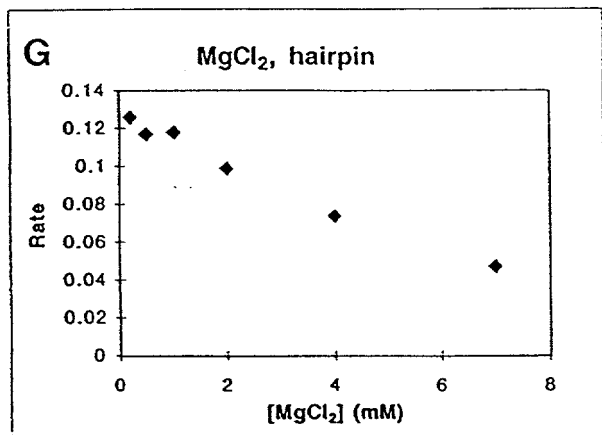
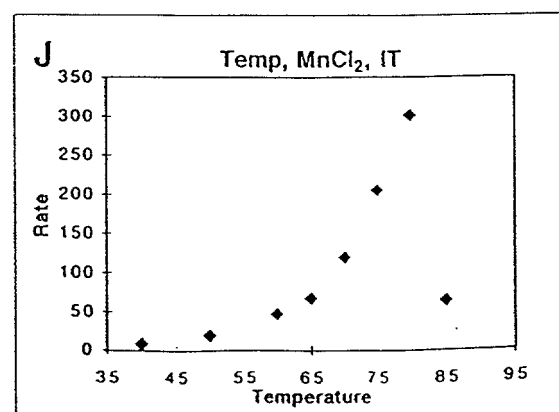
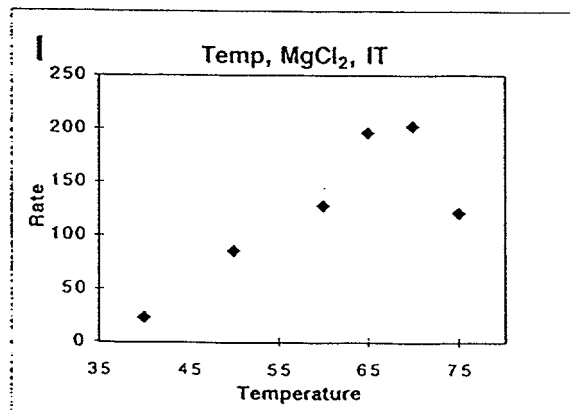
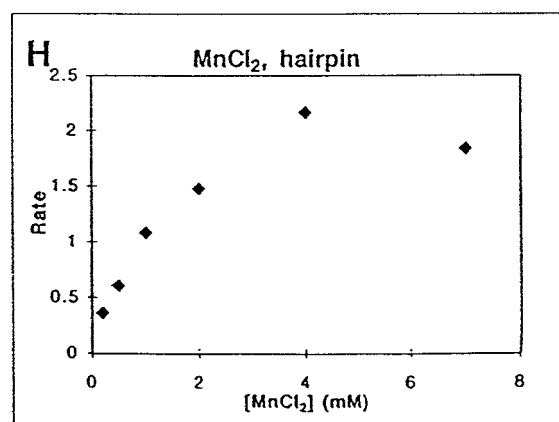
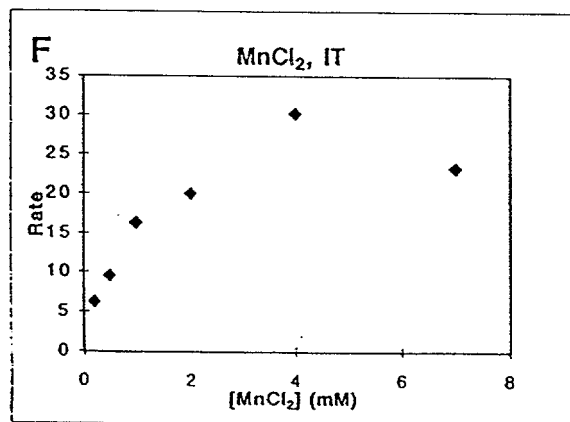
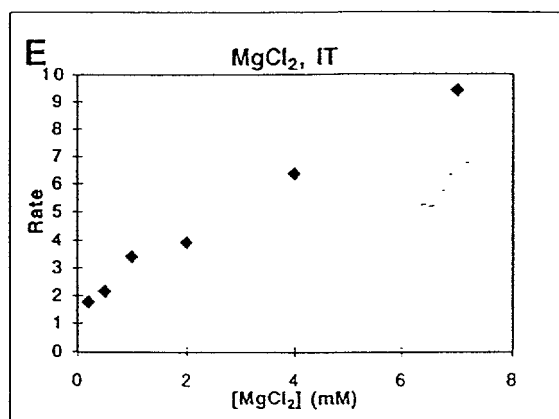
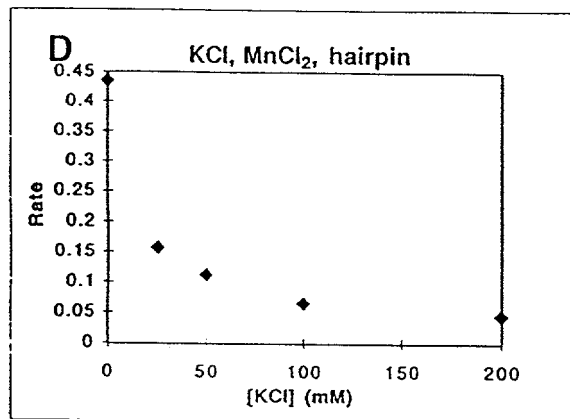
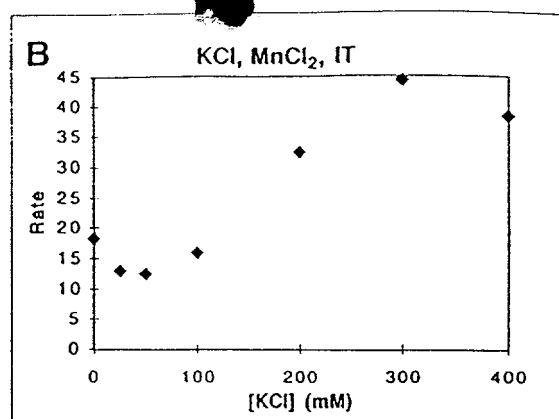
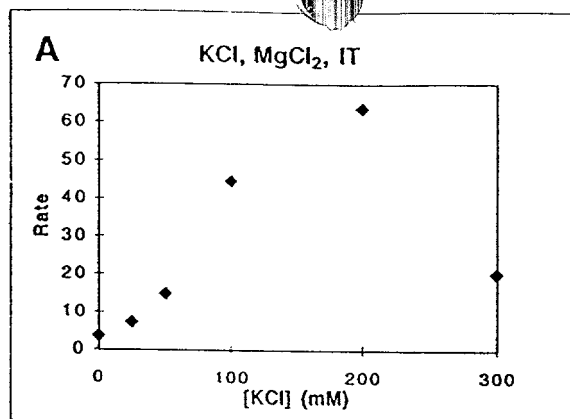
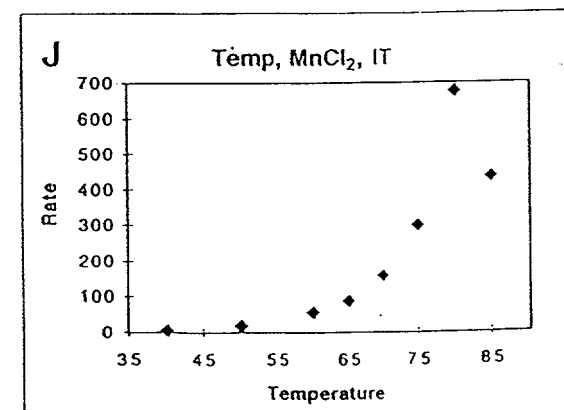
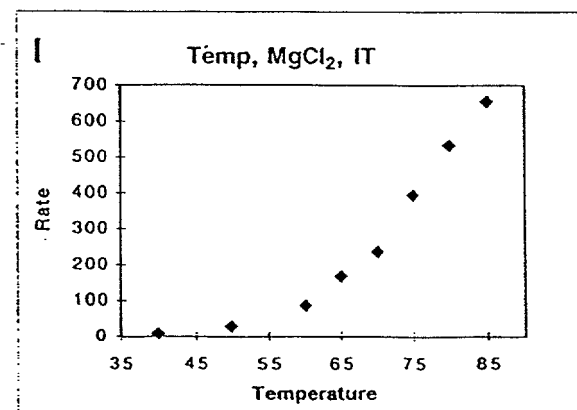
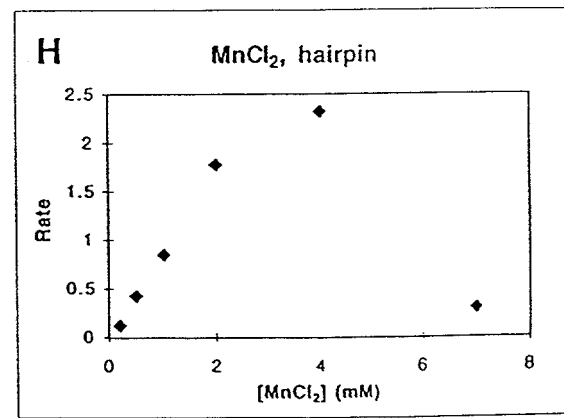
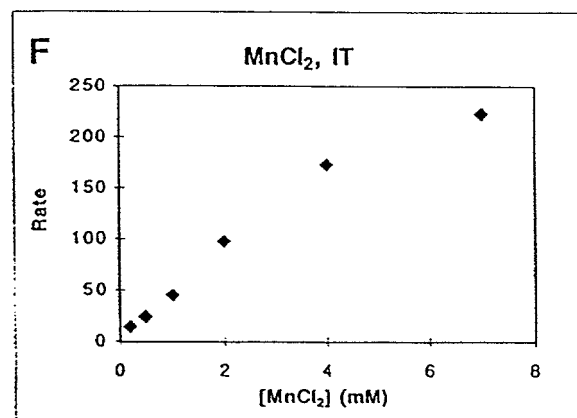
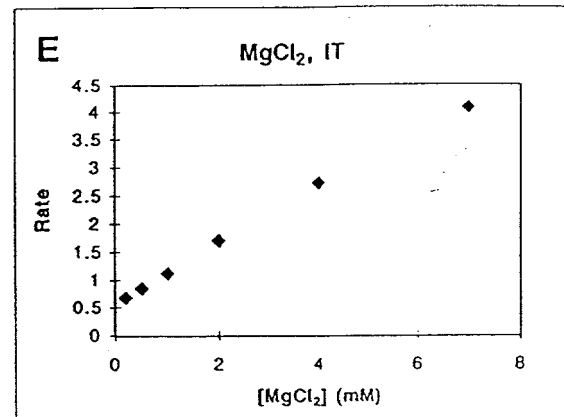
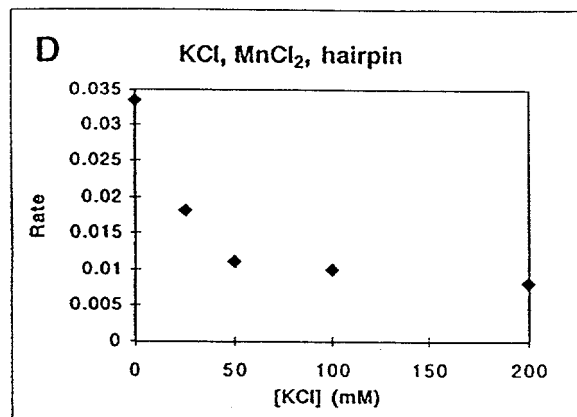
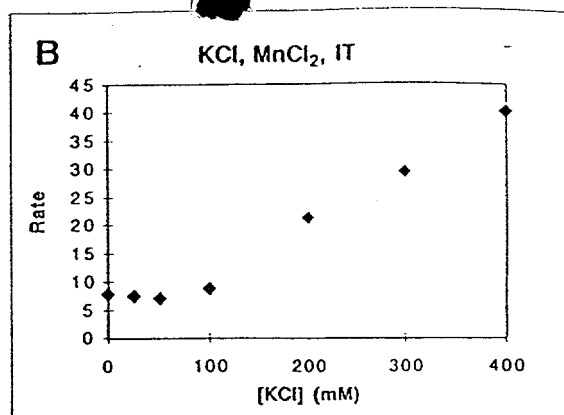
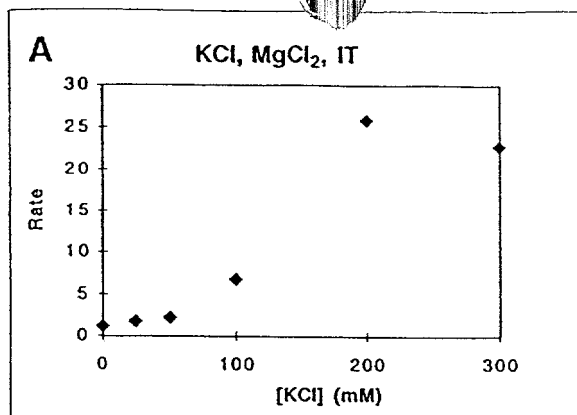


FIGURE 101



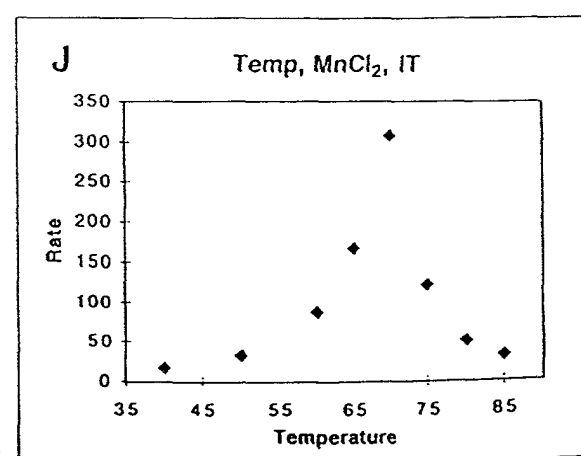
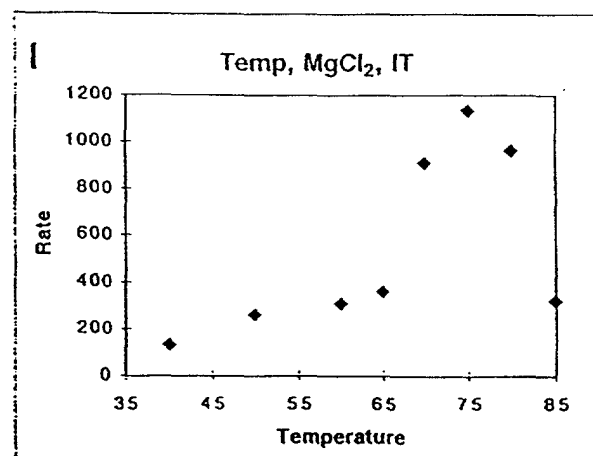
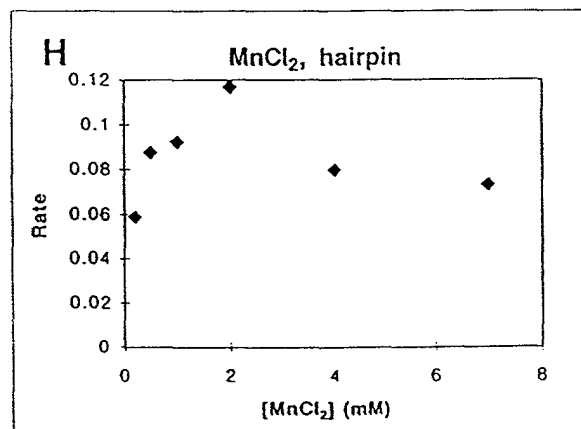
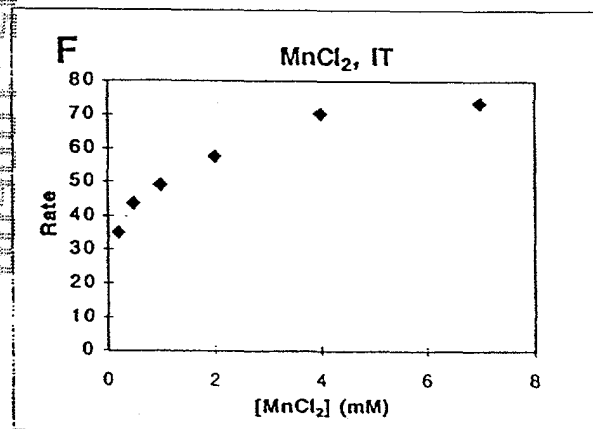
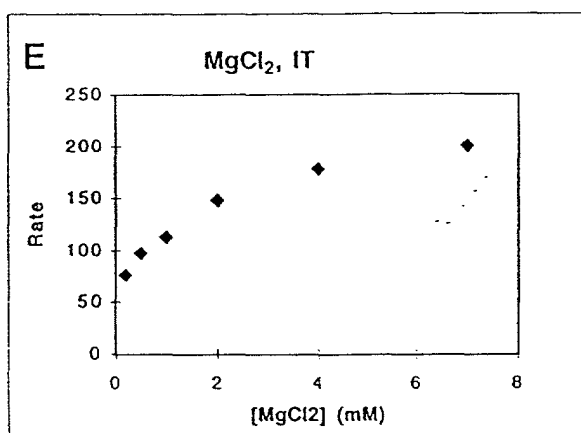
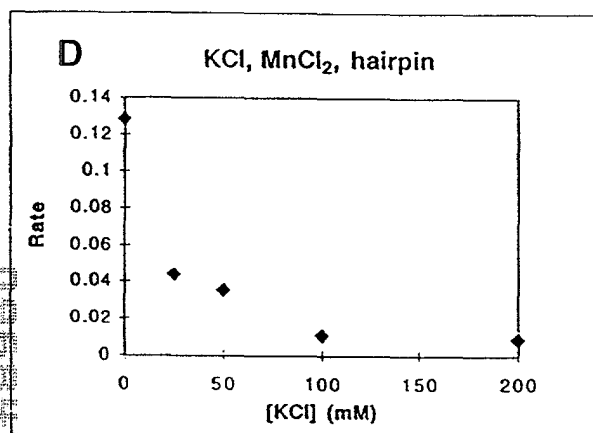
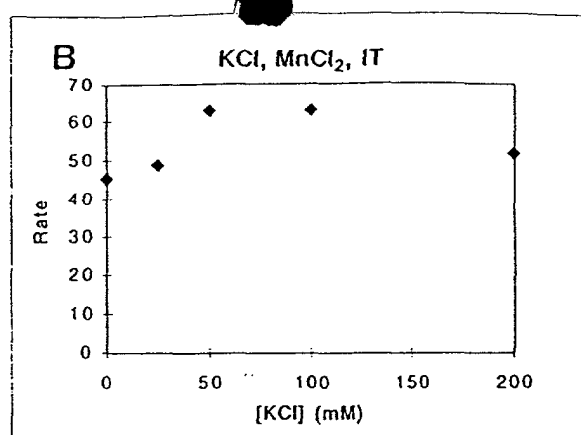
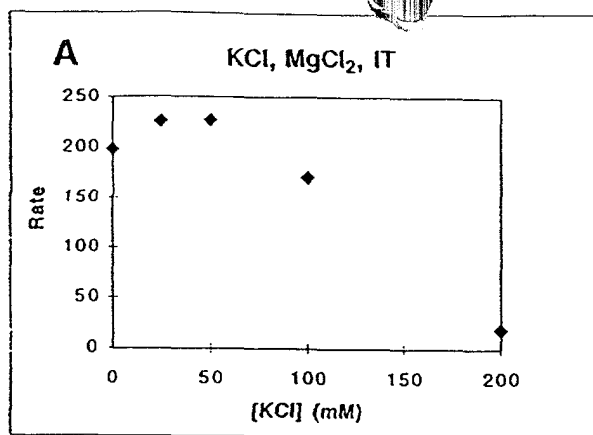
119/127

FIGURE 102



120/127

FIGURE 103



12/1/27

FIGURE 104

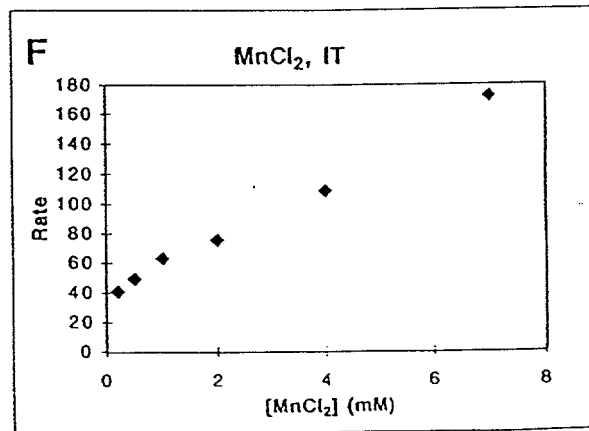
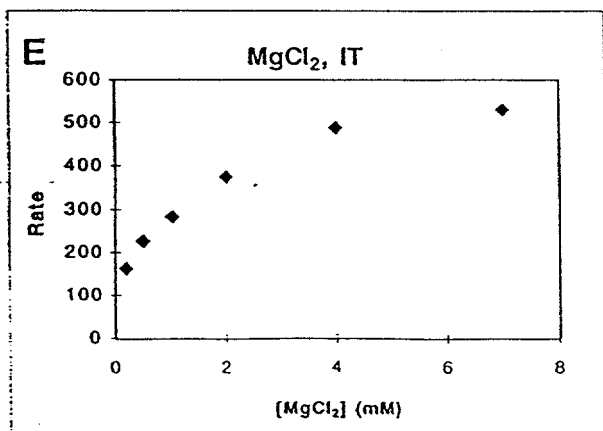
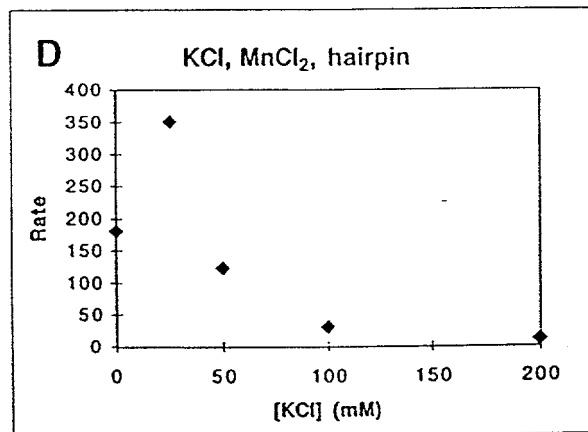
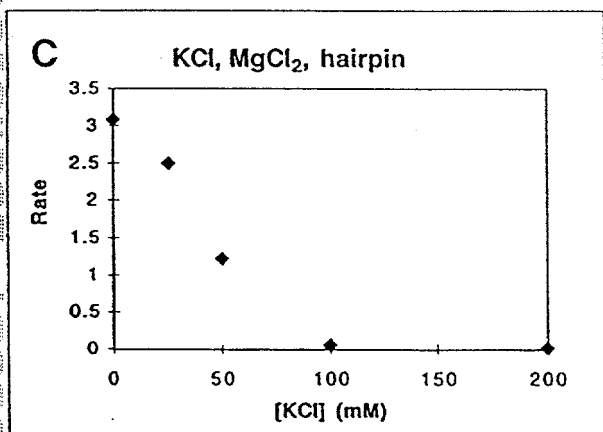
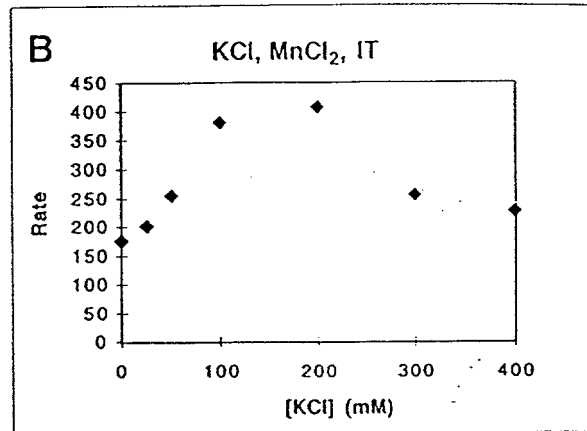
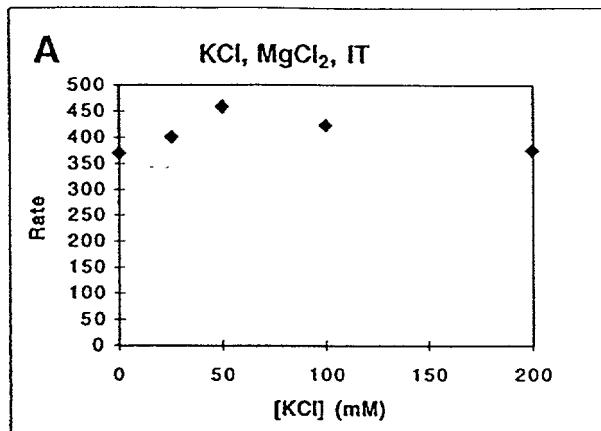


FIGURE 104 (cont.)

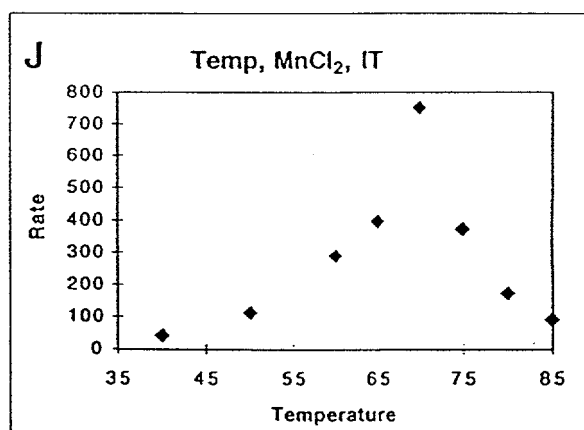
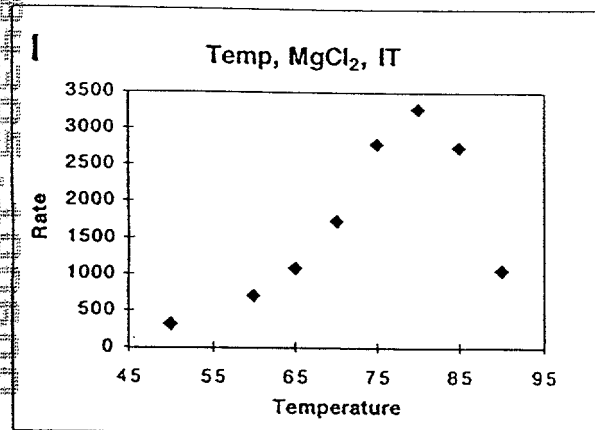
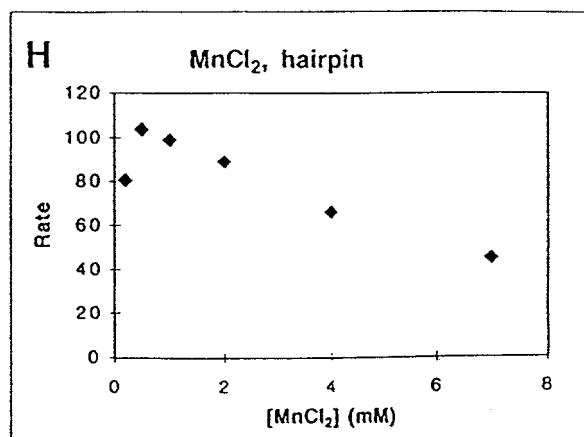
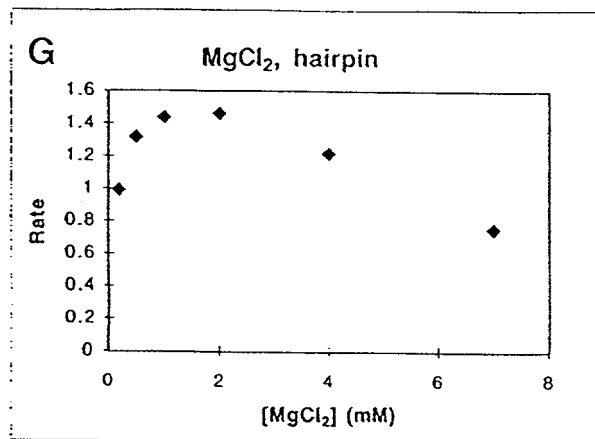


FIGURE 105

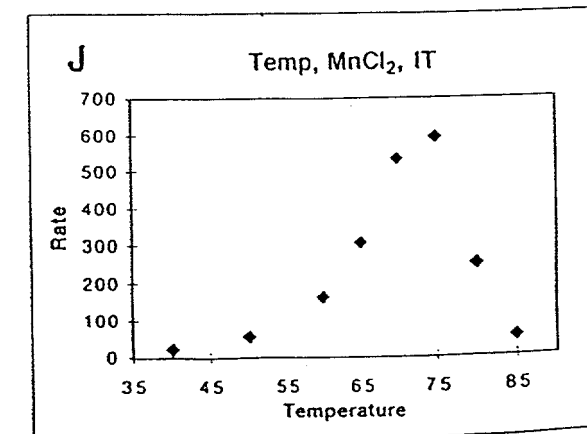
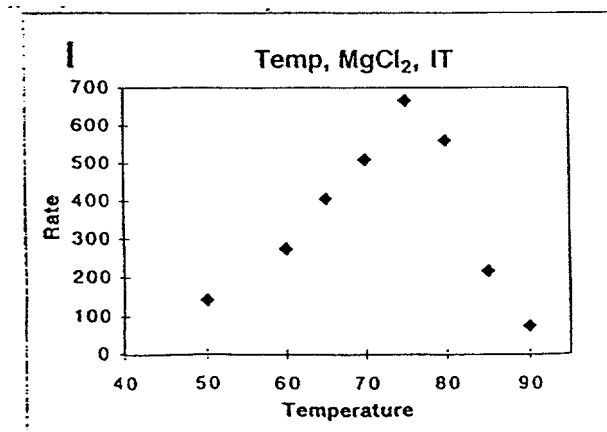
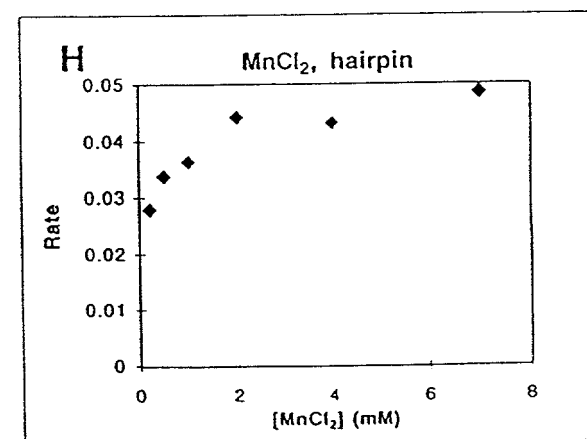
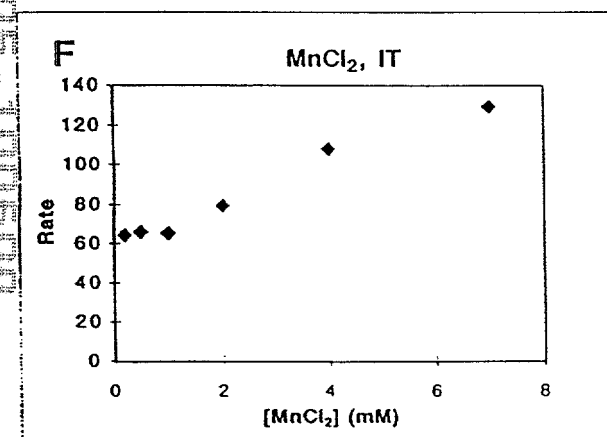
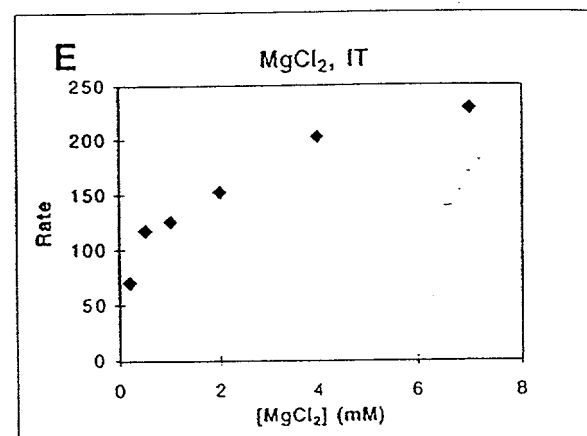
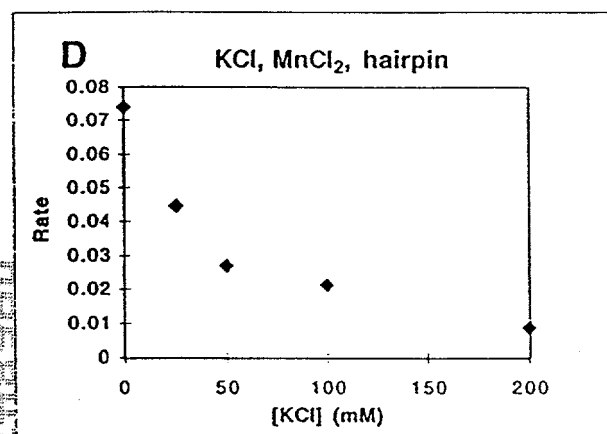
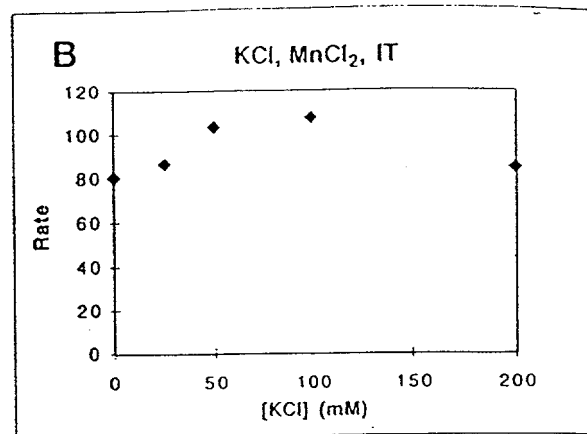
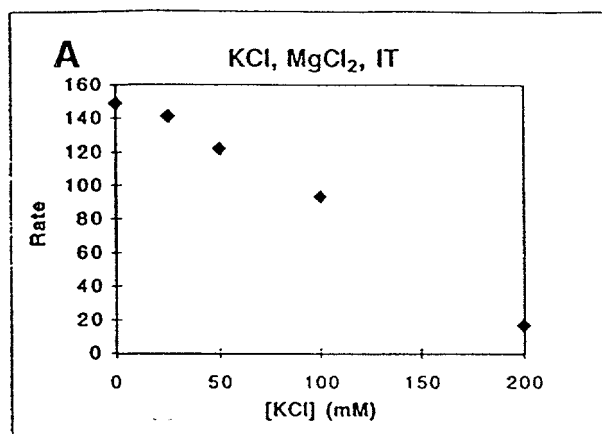


FIGURE 106

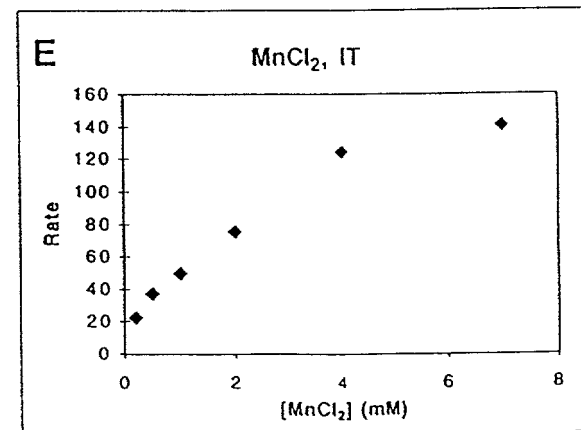
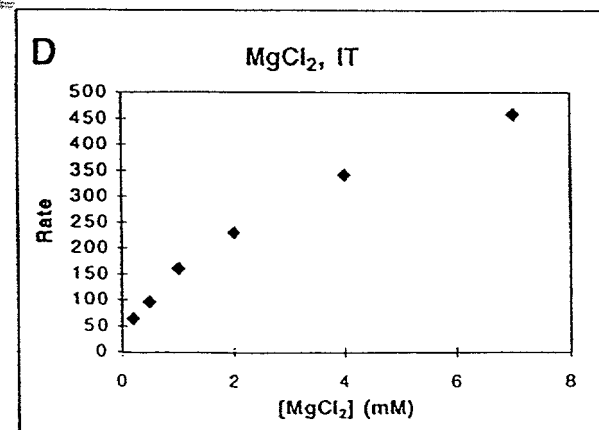
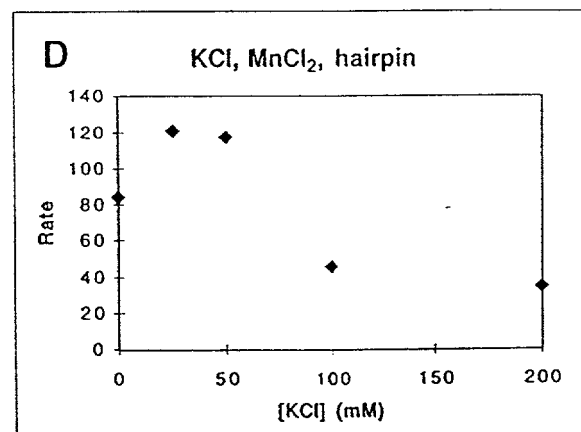
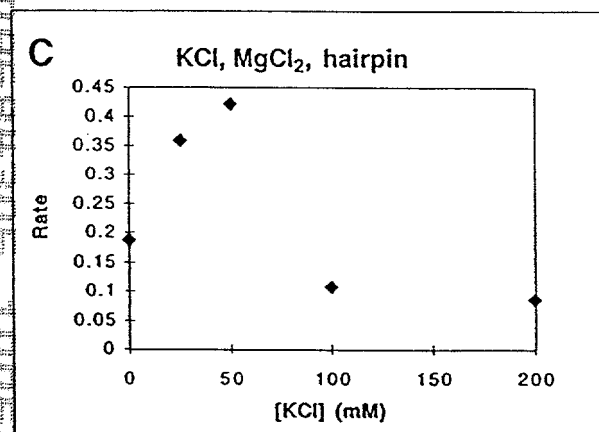
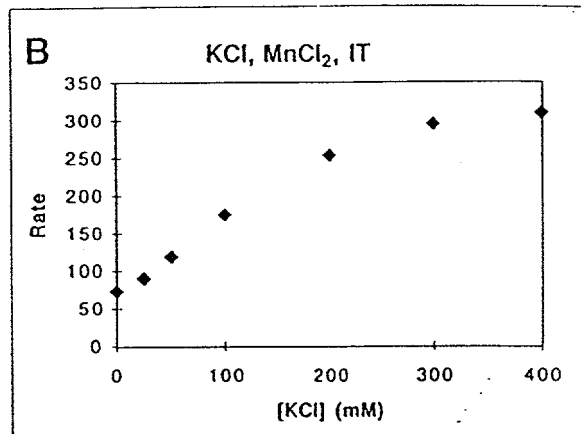
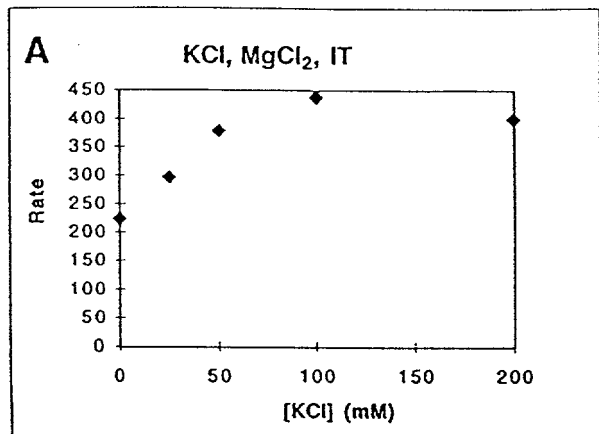


FIGURE 106 (cont.)

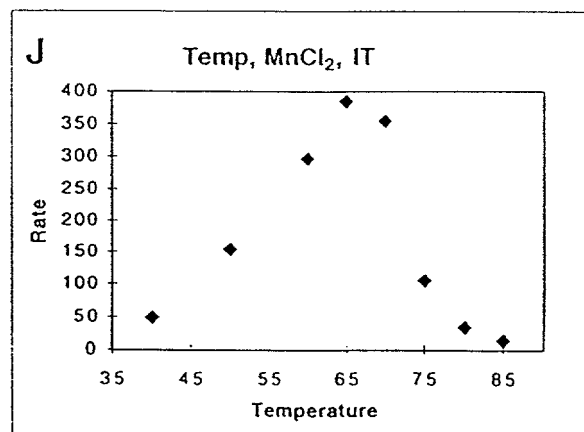
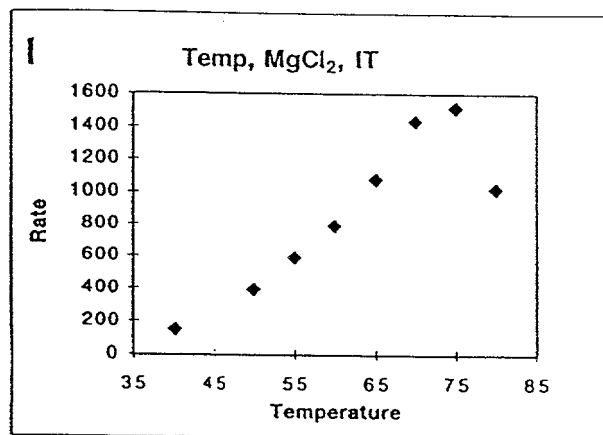
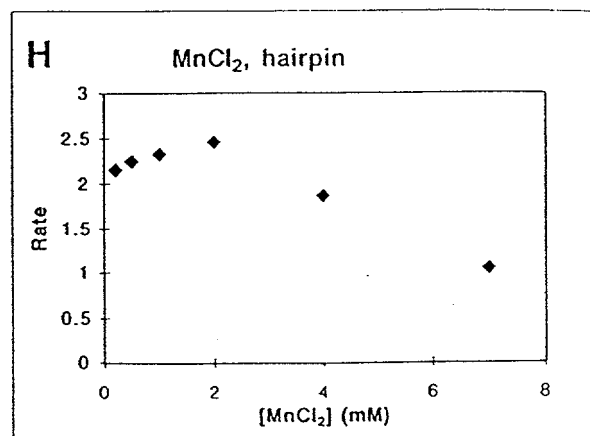
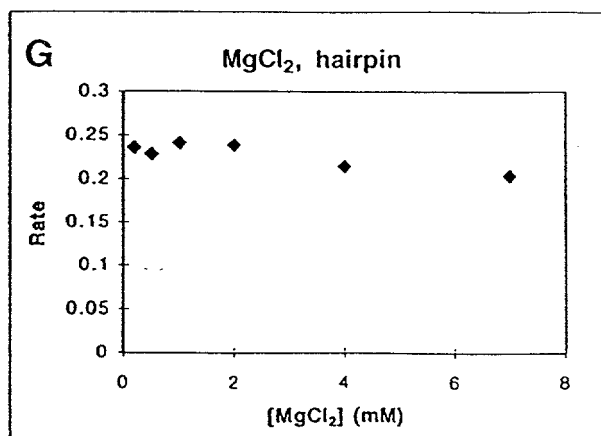
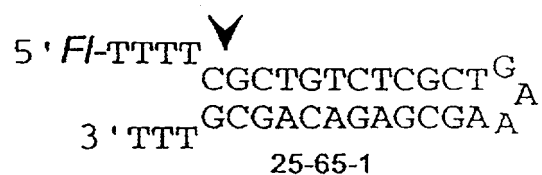


FIGURE 107

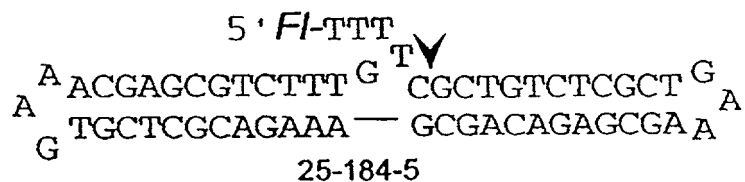
Hairpin Substrate

A)



B)

Invader (IT) substrate



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